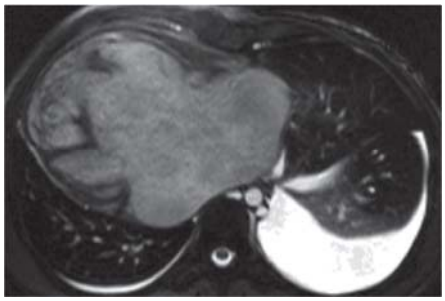
Why I Should Care About the Right Heart

Jonathan Lindner, MD

Slides not provided

Adult Congenital Heart Disease (ACHD): What Every Provider Should Know



Abigail Khan, MD, MSCE
Associate Clinical Chief of Cardiology
Co-director of the Maternal Cardiac Program
Oregon Health and Science University
No disclosures

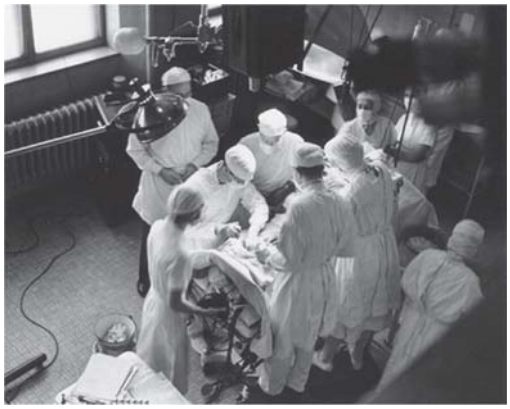
Spectrum of ACHD complexity

LOWEST → HIGHEST

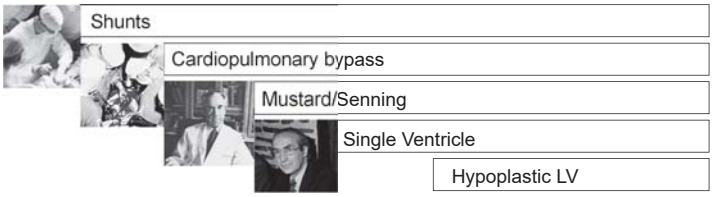
Simple	Moderate	Great complexity
AV disease	PAPVR, TAPVR	Conduits
MV disease*	AV Canal	Cyanotic CHD
PFO	Coarctation	Double outlet RV
Small ASD or VSD	Ebstein's	Fontan
Repaired PFO, ASD, VSD	Sinus venosus ASD	Eisenmenger
Mild PS	Primum ASD	PVOD
	Tetralogy of Fallot	TGA
	RVOT obstruction	Truncus arteriosus
	Significant PV disease	Heterotaxy

Warnes. The changing profile of CHD in adult life. JACC 2001

1944



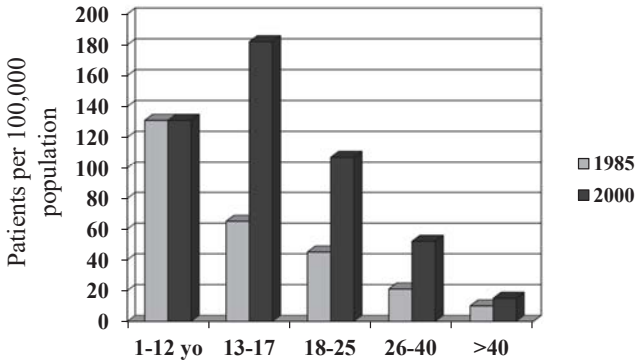
Evolution of Surgical Successes



10% SURVIVAL

90% SURVIVAL

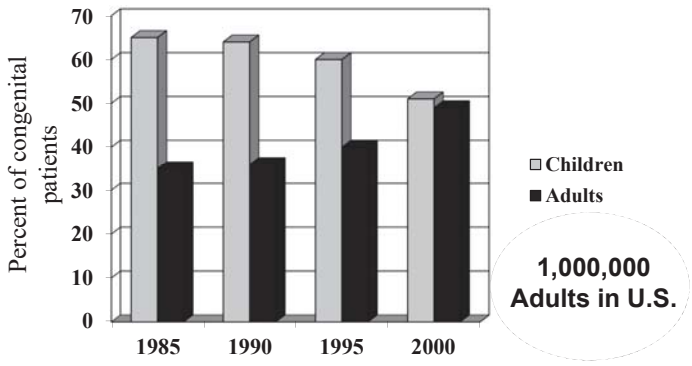
Adults = Children with CHD



Marelli A, Circulation. 2007;115:163-172

Adults = Children with CHD

Individuals with moderate/severe congenital heart disease



Marelli A, Circulation. 2007;115:163-172

Prevalence

Prevalence of medical conditions among "healthy" volunteers:

Abnormal LFTs	1.9%
Anemia	1.2%
Hyperlipidemia	1.1%
ACHD	0.8%
EtOH abuse	0.6%
Thyroid disease	0.5%
Vasovagal syncope	0.13%

Singh SD, Br J Clin Pharmacol 1999 July; 48(1):25-31

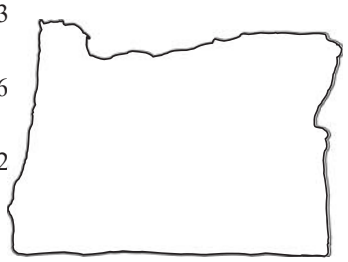
Prevalence of ACHD

Oregon Population 4,190,713

Congenital Heart Disease 33,526

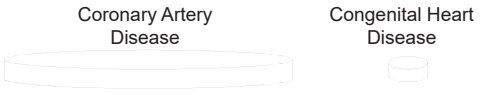
Adults with CHD 16,762

- 50% Portland Metro
- 30% Other Metro
- 20% Rural

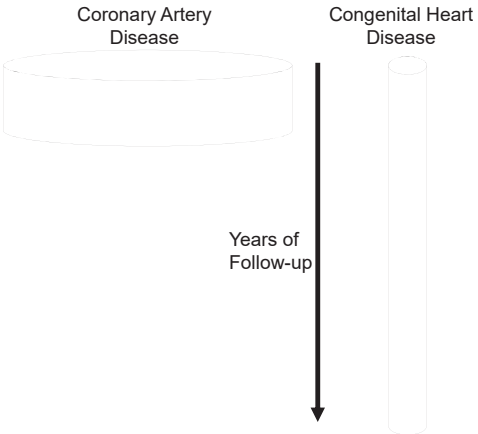


Khan and Broberg, unpublished data, 2019

Magnitude of Care



Magnitude of Care



Hoffman, JACC 2002

Journal of the American College of Cardiology
© 2005 by the American College of Cardiology Foundation
Published by Elsevier Inc.

STATE-OF-THE-ART PAPER

The Adult With Congenital Heart Disease

Born to Be Bad?

Carole A. Warnes, MD, MRCP, FACC
Rochester, Minnesota

ACHD Guidelines (2018)

Circulation

AHA/ACC GUIDELINE

2018 AHA/ACC Guidel of Adults With Congei

A Report of the American Coll Association Task Force on Clini

3.3. Delivery of Care

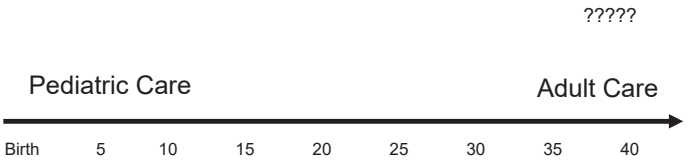
Recommendations for Delivery of Care
Referenced studies that support recommendations are summarized in Online Data Supplements 3, 4, and 5.

COR	LOE	Recommendations
I	B-NR	1. Patients with ACHD AP classification III-D, IIA-D, and IIA-D* should be managed in collaboration with an ACHD cardiologist.
I	C-LD	2. Cardiac surgery, catheter-based interventional cardiac procedures, and electrophysiological procedures involving congenital heart lesions in patients with ACHD should be performed by operators with expertise in CHD procedures and in collaboration with an ACHD cardiologist.

*See Tables 3 and 4 for details on the ACHD Anatomic and Physiological classification system.

All patients except those with repaired simple lesions and no hemodynamic or anatomic sequelae, including arrhythmias, should be seen in an ongoing manner by an ACHD cardiologist.

Where Are These Patients?



"Lost to Follow Up"

Children and Adults With Congenital Heart Disease Lost to Follow-Up
Who and When?

Andrew S. Mackie, MD, SM; Raluca Ionescu-Ittu, MSc; Judith Therrien, MD; Louise Pilote, MD, MPH, PhD; Michal Abrahamowicz, PhD; Ariane J. Marelli, MD

Background—Many patients with congenital heart disease (CHD) require lifelong care. However, the duration of cardiology follow-up in children and adults with CHD is unknown. We sought to determine the proportion of children and young adults with CHD receiving outpatient cardiology care and to identify predictors of lack of follow-up.
Methods and Results—The study population consisted of individuals born in 1983 and alive at age 22 years who were diagnosed with CHD in Quebec, Canada, before 6 years of age (n=643). Patients and outpatient visits were identified with the use of the provincial physician's claims database. Three age groups were examined for the presence of outpatient cardiology follow-up: 6 to 12, 13 to 17, and 18 to 22 years. CHD lesions were classified as severe (n=84; 13%), simple shunts (n=390; 61%), and "other" lesions (n=169; 26%). Failure to receive cardiac follow-up after the 6th, 13th, and 18th birthday occurred in 28%, 47%, and 61%, respectively. Among those with severe lesions, only 79% were seen after the 18th birthday. However, the majority of subjects visited primary care physicians in all age groups, and 93% remained in contact with the healthcare system into early adulthood. Predictors of lack of cardiology follow-up in adulthood included male sex, a nonsevere lesion, and a history of follow-up outside a university hospital setting.
Conclusions—Lack of cardiology follow-up begins during childhood, even among those with severe lesions. This occurs despite patients being in contact with other healthcare providers. Improved communication with primary care physicians may reduce the proportion of patients lost to cardiac follow-up. (***Circulation.* 2009;120:302-309.**)

Key Words: adults ■ congenital heart disease ■ continuity of care ■ pediatrics

Why are these patients not being seen?

Patient Obstacles

Patient assumes "cure"
Poor communication from parents or pediatrician
Loss of previous health records
Gradual symptom onset
Lack of health insurance

System Obstacles

Provider assumes "cure"
Uninformed about specific potential problems
No prior records available
No reported symptoms
Symptoms ascribed to more common causes
Insurance or lack of
Distance to care

The Non-Cardiology Encounter

Why is recognizing ACHD potentially important

- Complaints or problems may be secondary to congenital defect

The Non-Cardiology Encounter

Why is recognizing ACHD potentially important

- Complaints or problems may be secondary to congenital defect
- Treatment options can be impacted by the congenital defect

The Non-Cardiology Encounter

Why is recognizing ACHD potentially important

- Complaints or problems may be secondary to congenital defect
- Treatment options can be impacted by the congenital defect
- Provides a chance to review patients cardiac status

The Non-Cardiology Encounter

Why is recognizing ACHD potentially important

- Complaints or problems may be secondary to congenital defect
- Treatment options can be impacted by the congenital defect
- Provides a chance to review patients cardiac status
- Provides a chance to get patient plugged back in to specialty care when necessary

Recognizing Congenital Heart Disease

History

Potentially worrisome

"I had a hole in my heart"
"I was a blue baby"
"I had surgery as a child"
"Some part was twisted/missing"

Less worrisome

"I had a murmur as a child"
"I had funny heart rhythms as a teenager"
"I had mitral valve prolapse"
"I had a hole closed with a catheter procedure"

Recognizing Congenital Heart Disease

Concerning Symptoms

Exercise intolerance
Can't climb stairs
Can't do same activity as last year
Fever, especially recurrent
Prolonged palpitations
Syncope

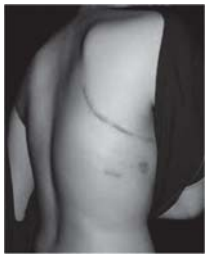
Less Concerning

Chest pain
Skipped beats/extra beats
Fatigue

Recognizing Congenital Heart Disease

Clinical Exam

Thoracotomy scar
Coarctation of the aorta
Conotruncal abnormalities
Tetralogy of Fallot
Pulmonary atresia
Truncus arteriosus
Anomalous pulmonary veins
Sternotomy scar
Everything else



Addressing Potential Problems

What are the major long-term complications to be aware of?

What are the high risk flags for predicting those complications?

Is their cardiac condition manifesting itself in non-cardiac ways?

Is management of a non-cardiac condition going to be affected by their cardiac condition?

Should I refer the patient for specialty care?

Cases

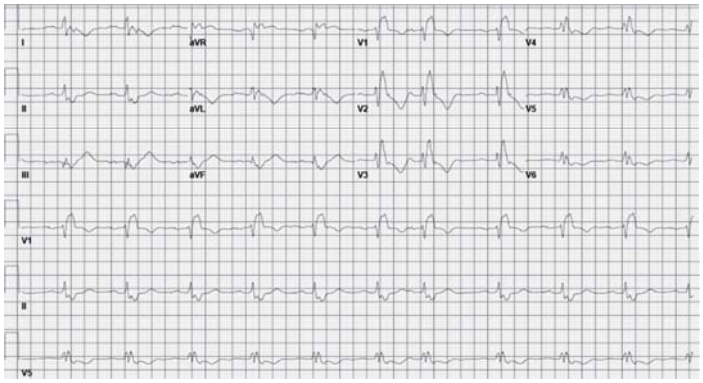
Case 1

36 year old woman had a "hole in my heart" as a kid
Surgery at age 3, doesn't know details.

No problems since that time
Followed by local cardiologist for murmur
"Mild pulmonary stenosis" on echo
Asymptomatic, walks several miles a day

Case 1

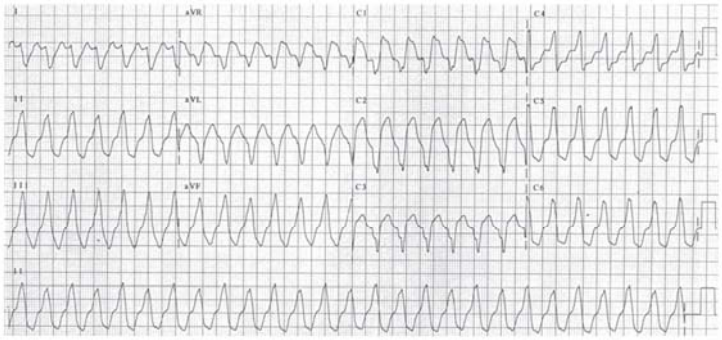
36 year old woman had a "hole in my heart" as a kid



Right Bundle Branch Block

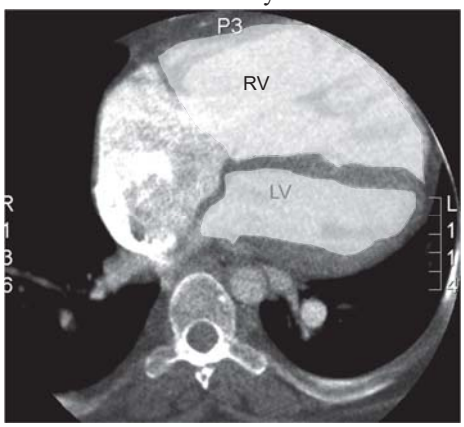
Case 1

36 year old woman had a "hole in my heart" as a kid
Presented with sudden diaphoresis and light headedness



Case 1

36 year old woman had a "hole in my heart" as a kid



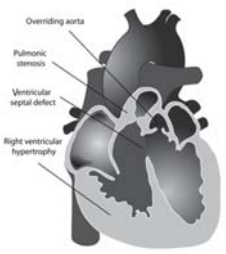
Case 1: Tetralogy of Fallot

Can be completely asymptomatic

Tetralogy of Fallot

Typical repair:
- VSD closure
- Relief of pulmonic stenosis
  - Typically affects the integrity of the pulmonary valve (e.g. transannular patch)

Long-term risks:
- Pulmonary regurgitation, often severe
- RV enlargement and eventual dysfunction
- LV dysfunction
- Arrhythmias
- Residual VSD (endocarditis)



Case 1

36 year old woman had a "hole in my heart" as a kid

Severe pulmonary valve regurgitation
Severely enlarged right ventricle

Adults with Congenital Heart Disease (ACHD)

Case 1

36 year old woman had a "hole in my heart" as a kid

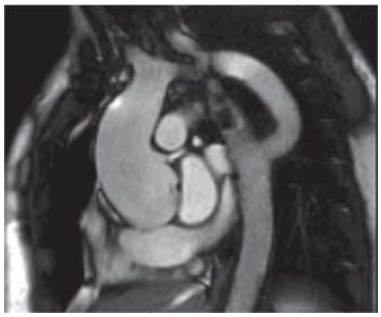
Patient underwent surgery to replace the pulmonary valve.
Implanted Cardioverter-Defibrillator.

1 year later
- Reduction of RV volume but not back to normal levels
- Has recurrent chest pain and frequent arrhythmia

Adults with Congenital Heart Disease (ACHD)

Case 2

33 year old with prior coarctation repair
- Surgical correction at one month of age
- Several corrective surgeries from complications related to his initial repair.



Adults with Congenital Heart Disease (ACHD)

Case 2

33 year old with prior coarctation repair
- Surgical correction at one month of age
- Several corrective surgeries from complications related to his initial repair.

Extensive story of his first 6 months of life well-documented
Patient very knowledgeable of the details
Had regular follow up

Adults with Congenital Heart Disease (ACHD)

Case 2

33 year old with prior coarctation repair

Presents to local ED with violent hematemesis/hemoptysis
"I splattered the bathroom wall with blood."

Adults with Congenital Heart Disease (ACHD)

Case 2

33 year old with prior coarctation repair

Presents to local ED with violent hematemesis/hemoptysis
"I splattered the bathroom wall with blood."

Work-up showed stable vital signs
Told it was probably epistaxis
Discharged

Case 2

33 year old with prior coarctation repair

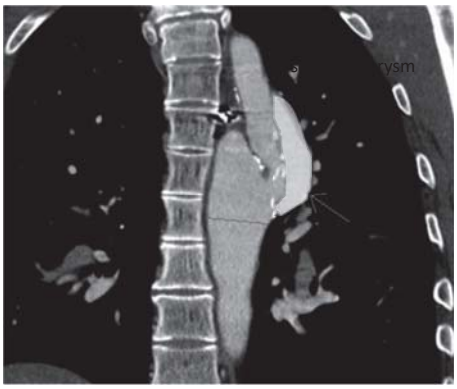
Presents to local ED with violent hematemesis/hemoptysis
"I splattered the bathroom wall with blood."

Work-up showed stable vital signs
Told it was probably epistaxis
Discharged

D-Dimer results positive; called back from parking lot

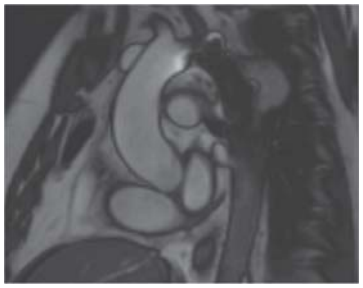
Case 2

33 year old with prior coarctation repair
CT scan to exclude pulmonary embolism



Case 2

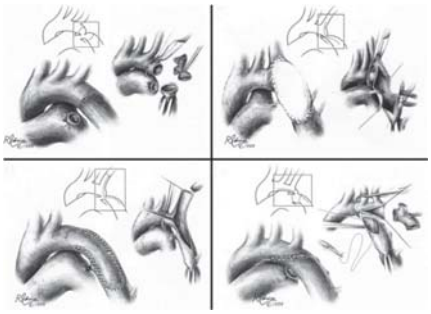
33 year old with prior coarctation repair
Life flight to referral center
Emergent covered stent deployment in the OR



Aortic coarctation

Variety of repairs

Long-term risks:
- Hypertension
- Recoarctation
- Aortic aneurysm or pseudoaneurysm
- Cerebral aneurysms



Torok et al. World Journal of Cardiology 2015; 26: 7(11): 765-775

Transposition of the Great Arteries

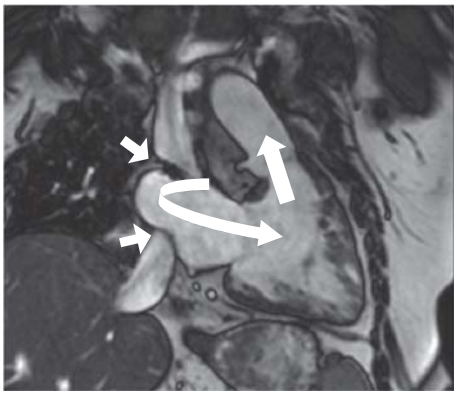
Two Distinct Subtypes

D-TGA	L-TGA
"[illegible]n"	
"Mustard" or "Senning"	Ventricular inversion
Atrioventricular concordance	Atrioventricular ***discordance***
Ventriculoarterial ***discordance***	Ventriculoarterial ***discordance***

RV is the systemic ventricle, predisposing to RV failure, TR, arrhythmias, heart failure

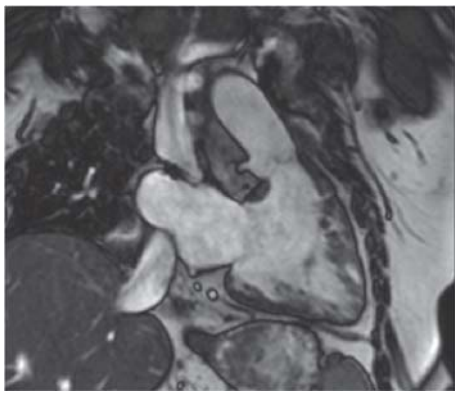
Transposition of the Great Arteries

Atrial Switch Palliation ("Mustard" or "Senning")



Transposition of the Great Arteries

Atrial Switch Palliation ("Mustard" or "Senning")



Transposition of the Great Arteries

Atrial Switch Palliation ("Mustard" or "Senning")

Common long-term problems:

- Obstruction of the venous pathways
- Atrial arrhythmia
- Tricuspid valve ("mitral") regurgitation
- Heart failure from systolic dysfunction

Case 3

41 year old with prior "Mustard" surgery

No surgery since then, generally healthy

Case 3

41 year old with prior "Mustard" surgery

No surgery since then, generally healthy

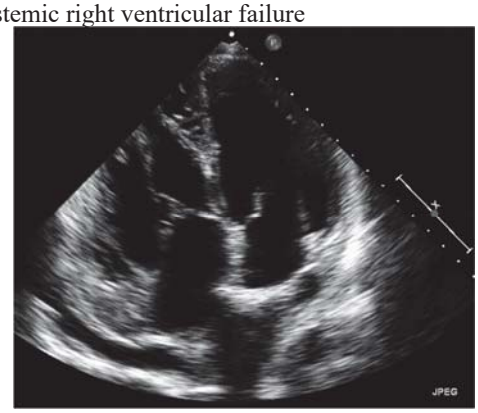
Gradually becoming more "out of shape"

Has gained 10 lbs in three months

Case 3

41 year old with prior "Mustard" surgery

Severe systemic right ventricular failure



Case 3

41 year old with prior "Mustard" surgery

Refractory heart failure

Several admissions

Worsening exercise capacity

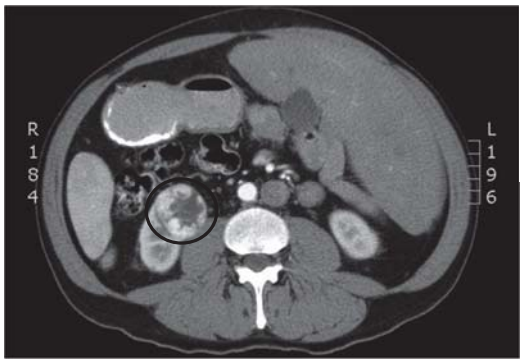
Referred for transplantation

Workup for listing began

Case 3

41 year old with prior "Mustard" surgery

Screening CT scan before heart transplant



Case 3

41 year old with prior "Mustard" surgery

Renal Cell Carcinoma
- Successful L nephrectomy
- No extension of tumor

Case 3

41 year old with prior "Mustard" surgery

Renal Cell Carcinoma
- Successful L nephrectomy
- No extension of tumor
- Not a transplant candidate
- Continued to have worsening heart failure

Case 3

41 year old with prior "Mustard" surgery

Renal Cell Carcinoma
- Successful L nephrectomy
- No extension of tumor
- Not a transplant candidate
- Continued to have worsening heart failure
- Eventually ventricular assist device placed
- Died two years later

Cancer in Congenital Heart Disease?

Frequent radiation exposure in childhood

Associated with increased long-term risk of malignancy

JAMA Network | Open.

Original Investigation | Cardiology

Risk of Cancer Among Children and Young Adults With Congenital Heart Disease Compared With Healthy Controls

Zacharias Mandalenakis, MD, PhD; Christina Karazisi, MD; Kristofer Skoglund, PhD; Annika Rosengren, PhD; Georgios Lappas, MSc; Peter Eriksson, PhD; Mikael Dellborg, PhD

Mean age of population late 20s
- 2.0% risk of malignancy in CHD patients
- 0.9% risk in controls
- Should these patients be screened?

Mandelenakis et al. JAMA Network Open 2019

What about pregnancy?

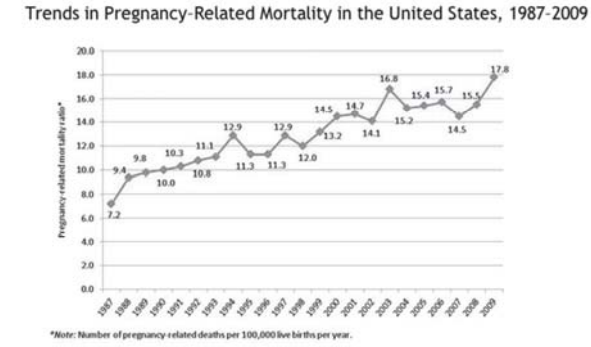
Study of pre-pregnancy counseling in ACHD

	Preferred Recommendation	
Advice Received	Pregnancy SAFE	Pregnancy UNSAFE
Pregnancy SAFE	80	9
Pregnancy UNSAFE	18	9

30% of women given wrong advice!

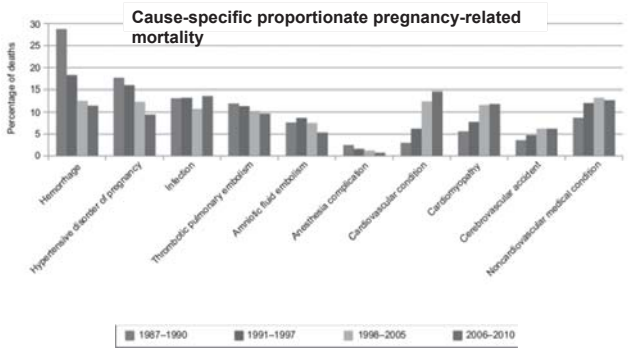
Kovacs, AH, JACC 2008 52(7):577-8

Mortality in pregnancy



http://www.cdc.gov/reproductivehealth/MaternalInfantHealth/PMSS.html#n8

CV disease is a significant contributor



Creanga et al. Obstet Gynecol 2015; 125: 5-12

Pregnancy risk in ACHD

- Most can carry a pregnancy safely
- Specialized care is key
- Risk parallels complexity of disease

WHO Class	Associated Risk	Lesion
I	**No detectable increased risk of maternal mortality and no/mild increase in morbidity.**	Uncomplicated, small or mild pulmonary stenosis, patent ductus arteriosus (PDA), mitral valve prolapse
		Repaired simple lesions: ASD or VSD, PDA, anomalous pulmonary venous drainage
		Isolated ectopic beats
II	**Small increased risk of maternal mortality or moderate increase in morbidity.**	Unoperated ASD or VSD
		Repaired tetralogy of Fallot
		Most arrhythmias
II or III	**May fall into higher or lower risk classification based on additional patient factors.**	Mild left ventricular impairment
		Hypertrophic cardiomyopathy
		Native or tissue valvular heart disease not considered class I or IV
		Marfan syndrome without aortic dilation
		Bicuspid aortic valve aortopathy with aorta < 45 mm
		Repaired coarctation
III	**Significantly increased risk of maternal mortality or severe morbidity.**	Mechanical valve
		Systemic right ventricle
		Fontan circulation
		Unrepaired cyanotic heart disease
		Other complex CHD
		Marfan syndrome with aorta of 40-45 mm
		Bicuspid aortopathy with aorta 45-50 mm
IV	**Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated.**	Pulmonary arterial hypertension
		Severe systemic ventricular dysfunction
		Peripartum cardiomyopathy with residual left ventricular dysfunction
		Severe mitral stenosis
		Severe symptomatic aortic stenosis
		Marfan syndrome with aorta dilated > 45 mm
		Bicuspid aortopathy with aorta > 50 mm
		Severe native coarctation

Combined Hormonal Contraception in Cardiac Disease

WHO Class 1 Always Use	WHO Class 2 Broadly Use	WHO Class 3 Caution with Use	WHO Class 4 Do not Use
MVP with trivial mitral regurgitation Bicuspid aortic valve with normal function Mild pulmonary stenosis Repaired coarctation with no HTN or aneurysm Simple congenital lesion successfully repaired in childhood with no sequelae	Most arrhythmias, other than a fib or flutter Uncomplicated mild native mitral and aortic valve disease Tissue prosthetic valve lacking features in class 3, 4 Surgically corrected congenital heart disease lacking features in class 3, 4 Small left-to-right shunts not reversible with physiologic maneuvers Hypertrophic cardiomyopathy lacking features in class 3, 4 Past cardiomyopathy fully recovered Uncomplicated Marfan	A fib or flutter on warfarin Bileaflet mechanic valves in the mitral or aortic position on warfarin ASD with left-to-right shunt that may reverse with physiologic stress Repaired coarctation with aneurysm and/or HTN Marfan with aortic dilation Previous thromboembolism Dilated left atrium > 4 cm	A Fib or flutter not anticoagulated Bjork-Shiley or Starr Edwards valves Pulmonary hypertension or pulmonary vascular disease Fontan heart Cyanotic heart disease Pulmonary AVM Past thromboembolic event not anticoagulated Prior left ventricular dysfunction Coronary artery disease Coronary arteritis

Slide courtesy of Dr. Lisa Bayer.

What Every Provider Should Know

ACHD patients are common

Prior surgery almost never means “cure.”

Many patients are receiving uninformed care or no care

Many have multisystem manifestations

ALL Providers should be aware of common pitfalls:

- Don’t ignore subtle but progressive problems
- Treat arrhythmias aggressively
- Avoid uninformed or unnecessary imaging
- Avoid uninformed advice
- Seek consultation

Common complications of CHD

Simple Shunts

Atrial septal defect	Arrhythmia, venous abnormalities, PAH
Ventricular septal defect	Endocarditis, PAH
Patent ductus arteriosus	No concerns
Atrioventricular septal defect	Heart block, LVOT obstruction, Mitral regurgitation
Anomalous pulmonary vein	Venous obstruction

Left-sided problems

Bicuspid valve	Enlarged aorta, valve dysfunction
Coarctation	HTN, recurrent obstruction
Sub-aortic stenosis	Recurrent obstruction
Cor-triatriatum	Arrhythmia

Right-sided problems

Pulmonic stenosis	Pulmonary regurgitation
Ebstein Anomaly	RV failure

Adults with Congenital Heart Disease (ACHD)

Common complications of CHD

Complex/Cyanotic Lesions

Tetralogy of Fallot	Pulmonary Regurgitation, Arrhythmia
Pulmonary Atresia	Pulmonary valve dysfunction, branch stenoses
Truncus arteriosus	Conduit dysfunction, aortic valve dysfunction
Transposition	Bradycardia, venous stenosis, pump failure
Eisenmenger syndrome	Hemoptysis, gout, arrhythmia
Single ventricle heart	Everything!!

Coronary artery anomalies

Anomalous origin	Coronary Ischemia
Coronary fistulae	LV dysfunction

Aortopathy

Marfans	Aortic size, pregnancy concerns
Turners	Hypertension, pregnancy concerns, dissection

Adults with Congenital Heart Disease (ACHD)

Referring patients to OHSU

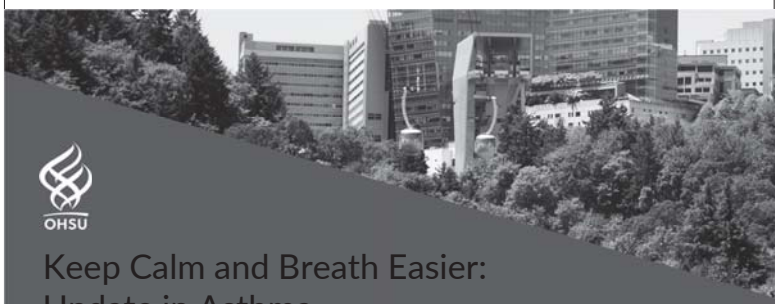
- Clinics in Portland, Eugene, Bend, and Boise
- Phone: (503) 494-7400
- Email: khaab@ohsu.edu
- https://www.ohsu.edu/knight-cardiovascular-institute/adult-congenital-heart-disease


Abigail Khan, MD


Craig Broberg, MD


Patricia Woods, NP


Adrienne Kovacs, PhD



Keep Calm and Breath Easier: Update in Asthma

SHYAM JOSHI, MD
ASSISTANT PROFESSOR OF MEDICINE
SECTION OF ALLERGY AND IMMUNOLOGY

DATE: FEBRUARY 12TH, 2020

Disclosures

- Advisory panel participant for GSK (2019)
- PRIME Lecturer (2019)

Objectives

- Describe recent advancements in asthma pathophysiology and management options.
- Categorize asthma based on phenotype and endotype.
- Review management changes in GINA guidelines.
- List biologic treatments available for asthma.

Outline

- Burden of Disease
- Diagnostic Guidelines
  - Spirometry
  - FeNO
- Management Options
  - Epinephrine inhalers
  - Asthma Phenotypes and Endotypes
  - Biologic therapies
- Asthma Mimickers

Asthma Definition

"Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation."

GINA 2018 Pocket Guidelines.

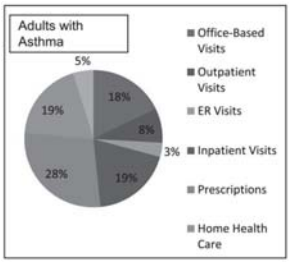
Asthma – Burden of Disease

- 7.3%-8.4% of the US population is affected by Asthma
  - ~23-27 million individuals
  - ~17-19 million adults
- Productivity Measure in Asthmatics
  - Lower odds of employment (OR 0.78)
  - Increased absent from work, sick in bed (IRR 1.33)
  - Increased odds of having activity limitations (OR 1.59)

Tran P and Tran L. *J Asthma*, 2018.
Moorman JE, et al. *Vital health Stat*, 2012.
Centers for Disease Control and Prevention. www.cdc.gov/asthma/nhis.
Sullivan PW, et al. *J Allergy Clin Immunol*, 2011.
NIH Morbidity and Mortality, 2007.

Asthma Healthcare Costs

- National economic burden of asthma: $18-56 billion
  - Direct costs
    - Medications, office visits, ED visits, hospitalizations, home health care
  - Indirect costs
    - Work absenteeism, missed school days
- 9th most expensive chronic disease to treat in the US



Sullivan PW, et al. *J Allergy Clin Immunol*, 2011.
CDC Chronic Disease Prevention and Health Promotion.

Diagnostic Guidelines

- Before treating, the correct diagnosis must be made
- GINA Guidelines
  1. Symptoms consistent with asthma?
  2. History consistent with asthma?
  3. Spirometry with reversibility testing
  4. Consider bronchial provocation testing

GINA 2018 Pocket Guidelines.

Spirometry

Choosing Wisely
An initiative of the ABIM Foundation

American Academy of Allergy, Asthma & Immunology

Five Things Physicians and Patients Should Question

5 Don't diagnose or manage asthma without spirometry.

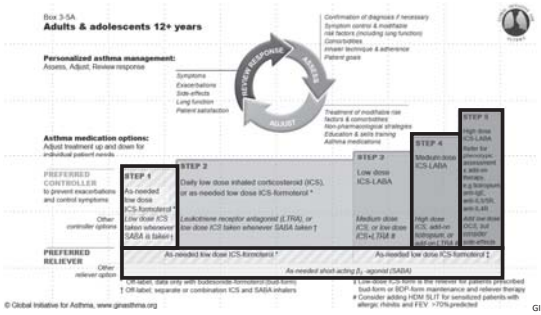
https://www.choosingwisely.org

Fractional Exhaled NO (FeNO)

- Not included in GINA guidelines
- Currently, management is titrated to symptom control
  - No correlation between symptoms and level of airway inflammation
- Sputum samples is gold standard for inflammatory phenotyping
- FeNO is a noninvasive, standardized diagnostic test to measure levels of airway eosinophilic inflammation

https://www.niox.com/en-us/niox-vero/about-niox-vero/

Management



GINA 2019 Pocket Guidelines.

ICS/formoterol vs SABA

SABA vs Epinephrine inhaler

Step 4 – Medium dose ICS/LABA

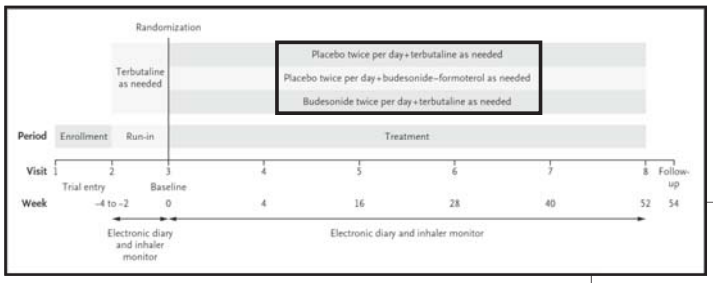
Biologic Therapy

ICS/LABA for Maintenance and Rescue

- Single Maintenance And Reliever Therapy (SMART)
  - Meta-analysis of 16 RTCs (22,748 patients)
  - Duration: 6-12 months
- Results – SMART vs ICS/LABA/SABA
  - Risk reduction of 6.4% for asthma exacerbation
    - Needs for systemic steroids, hospitalization or ED visit
  - No change in ACQ-5
  - No association with all-cause mortality
  - No association with changes in FEV1 or FVC
  - No difference in the number of rescue inhalations per day

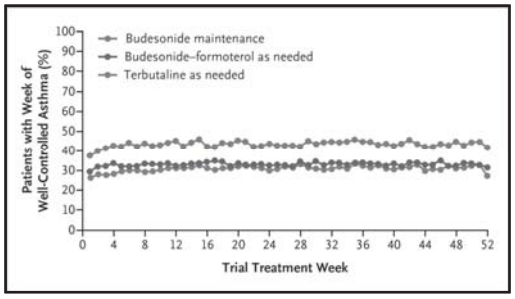
Sobieraj DM, et al. *JAMA*, 2018.

ICS/LABA for Rescue Only



O'Byrne PM, et al. *NEJM*, 2018.

ICS/LABA for Rescue Only



Median daily dose of inhaled glucocorticoid:	
Budesonide maintenance	340 µg
Budesonide-formoterol as needed	57 µg

O'Byrne PM, et al. *NEJM*, 2018.

ICS/LABA As Needed

- Role for using ICS/LABA for as needed therapy
  - Poor compliance
  - Aversion to inhaled steroids
  - Possibly in patients with very intermittent triggers (infections)
- Only with specific LABAs
  - Formoterol
  - Vilanterol
  - NOT Salmeterol

Epinephrine Inhaler

- Production halted in 2011
  - Chlorofluorocarbons (CFCs) propellant
- New FDA approval in late 2018 with hydrofluoroalkanes (HFAs) propellant
- Short acting bronchodilator
- Dosage: 1-2 puffs q4hr PRN

https://www.nbcnews.com/health/health-news/primatene-non-prescription-asthma-inhaler-back-after-7-years-n934106

Epinephrine Inhaler

Advantages

- More readily available
  - Low healthcare access areas
- Similar cost as albuterol

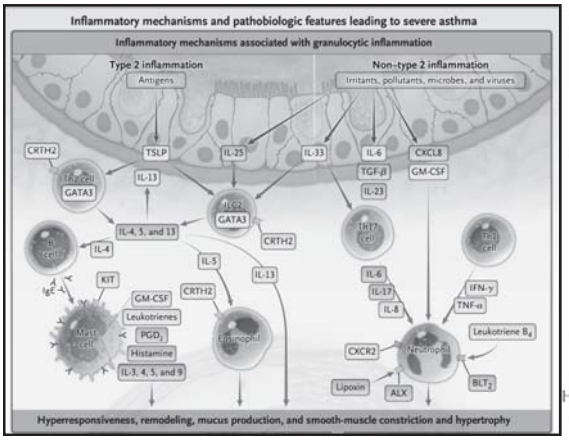
Disadvantages

- Possibly more significant side effect profile
- Confusion with IM epinephrine
- Use in non-asthmatic indications
  - Chronic cough, COPD
- Not indicated for children <12 years of age
- Self-management of asthma instead of establishing care with healthcare provider

Severe Asthma Phenotypes

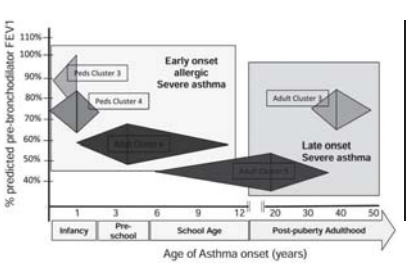
- >50% of patients have suboptimal asthma control
  - Multifactorial: Medication access/compliance, refractory phenotype
  - Decreased quality of life scores
  - Increased risk of life-threatening exacerbations
  - Increased healthcare costs and missed school/work days
- Subset of patients that do not respond appropriately to inhaled corticosteroids or even systemic steroids

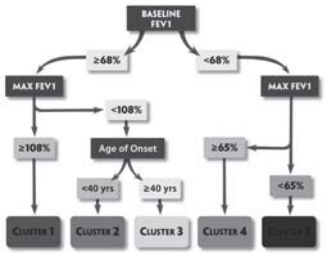
Fitzpatrick AM and Moore WC. *J Allergy Clin Immunol Pract*, 2017.



OREGON HEALTH & SCIENCE UNIVERSITY

Asthma Phenotypes





Fitzpatrick AM and Moore WC. *J Allergy Clin Immunol Pract*, 2017.

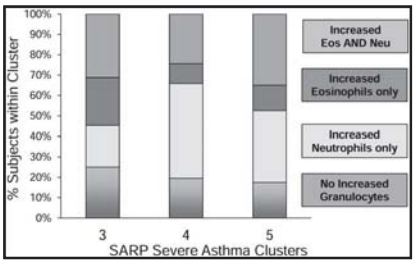
Clinical Asthma Phenotypes

Category	Phenotype
Trigger-induced asthma	(1) Allergic
	(2) Non-allergic
	(3) Aspirin-exacerbated respiratory disease (AERD)
	(4) Infection
	(5) Exercise-induced
Clinical presentation of asthma	(6) Pre-asthma wheezing in infants
	Episodic (viral) wheeze
	Multi-trigger wheezing
	(7) Exacerbation-prone asthma
	(8) Asthma associated with apparent irreversible airflow limitation
Inflammatory markers of asthma	(9) Eosinophilic and neutrophilic asthma

Kim H, et al. *Allergy Asthma Clin Immunol*, 2017.

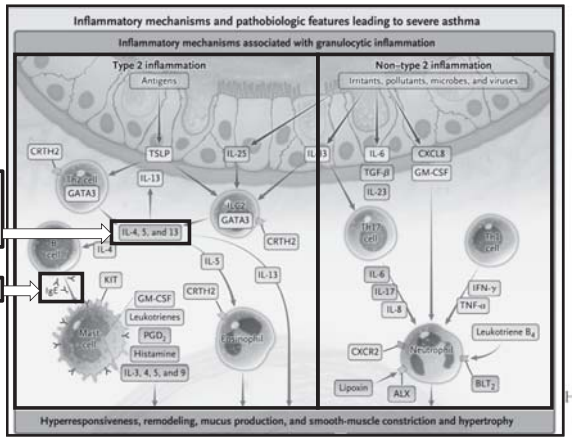
OHSU

Asthma Endotypes



Fitzpatrick AM and Moore WC. *J Allergy Clin Immunol Pract*, 2017.

OHSU



Mepolizumab
Reslizumab
Benralizumab
Dupilumab

Omalizumab

Israel, et al. N Engl J Med. 2017;377(10):965–976.

OREGON HEALTH & SCIENCE UNIVERSITY

Biologic Therapy

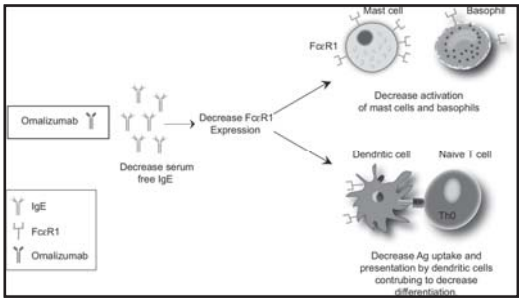
- Omalizumab (α-IgE mAb)
- Mepolizumab (α-IL-5 mAb)
- Reslizumab (α-IL-5 mAb)
- Benralizumab (α-IL-5 receptor mAb)
- Dupilumab (α-IL-4α receptor mAb)

FDA Approved

- Tezepelumab (α-TSLP mAb)
- Tralokinumab (α-IL-13 mAb)
- Lebrikizumab (α-IL-13 mAb)
- Pitrakinra (IL-4, IL-13 competitive antagonist)

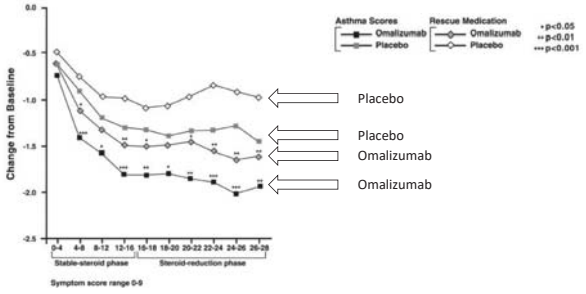
OHSU

Omalizumab



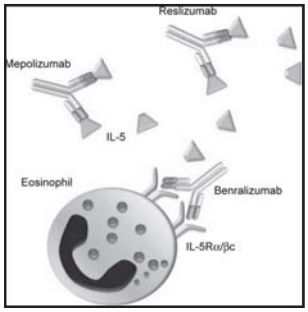
Tabatabaian F and Ledford DK. *J Asthma Allergy*, 2017.

Omalizumab Efficacy



Busse WW. *Am J Respir Crit Care Med*, 2001.

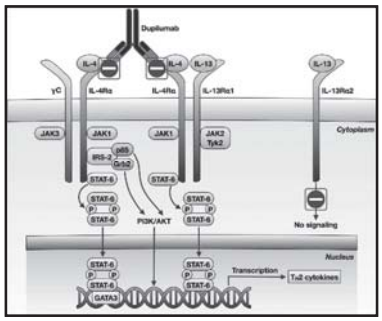
Anti-IL-5 Monoclonal Antibodies



- IL-5 promotes eosinophil differentiation, degranulation, survival, proliferation, chemotaxis, and adhesion
- Anti-IL-5 Therapy
  - Mepolizumab – EGPA
  - Reslizumab
- Anti-IL-5 Receptor Therapy
  - Benralizumab

Pelaia G, et al. *Ther Clin Risk Manag*, 2016.

Dupilumab



- FDA approved in 2018 for asthma
- Also has atopic dermatitis and nasal polyps indications
- Inhibits IL-4Rα
  - IL-4R and IL-13R
- Decreases signaling leading to decreased Th2 pro-inflammatory cytokines

Pelaia C, et al. *Exp Opin Biologic Ther*, 2017.

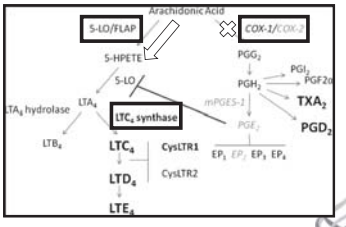
Asthma Biomarkers Available

- Total IgE levels
- Specific IgE to environmental allergens
  - Animals, pollen, dust mite, and molds
- Sputum samples
  - Eosinophils
  - Neutrophils
- Peripheral eosinophilia
- FeNO
- Periostin
- DPP-4

Kim H, et al. *Allergy Clin Immunol*, 2017.

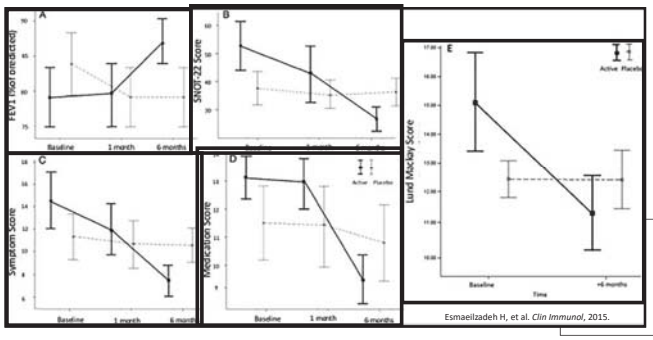
Aspirin Exacerbated Respiratory Disease (AERD/NERD)

- 2-9% of all adults with asthma have AERD
  - ~15% of all adults with severe asthma
- ~30% of all adults with asthma and nasal polyps have AERD
- Typically develops suddenly in adulthood
  - Between 20-50 years old
- 75% of patients with AERD will have mild-to-moderate respiratory symptoms with alcohol consumption



Kennedy JL, et al. *Am J Rhinol Allergy*, 2016.
Stevens W, et al. *Curr Allergy Asthma Rep*, 2015.

Aspirin Desensitization



Esmaeilzadeh H, et al. *Clin Immunol*, 2015.

Problems with Medication Compliance

- Reasons for nonadherence:
  - Difficulty with inhaler, cost of medications
  - Fear of side effects, actual side effects
  - Underestimation of severity, forgetfulness/complacency
  - Complex regimens, complicated work schedules
- Underuse and overuse of medications

OHSU

Improving Compliance

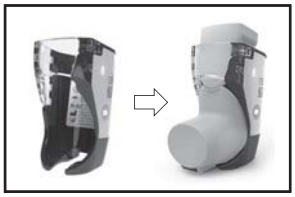
- Establishing partnership
- Identify barriers to adherence
  - Education
  - Financial
  - Complexity
  - Other stressors
  - Fear of medications
- Asthma action plans

National Asthma Council Australia, 2019.

OHSU

Digital Counters

https://www.propellerhealth.com/how-it-works/



https://www.hailie.com/products/

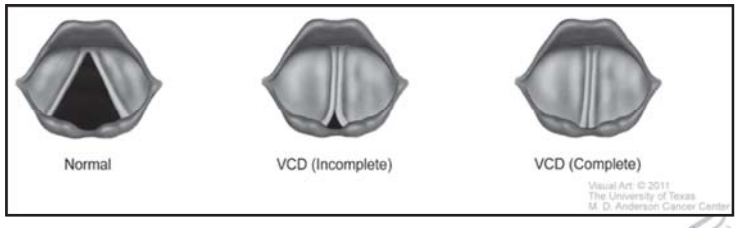
OHSU

Asthma Mimickers and Subtypes

- Vocal cord dysfunction (VCD)
- Reflux/LPR
- Non-asthmatic cough (chronic cough)
- Chronic obstructive pulmonary disease (COPD)
- Allergic bronchopulmonary aspergillosis (ABPA)
- Eosinophilic granulomatosis with polyangiitis (EGPA)
- Aspirin exacerbated respiratory disease (AERD)

OHSU

Vocal Cord Dysfunction



M.D. Anderson Cancer Center, 2011.

OHSU

Take Home Points

- Spirometry is essential in the diagnosis of asthma and should be performed before therapy is initiated (if possible)
- ICS/LABA in certain situations can be used as a PRN medication alone
- Asthma phenotypes and endotypes is the future of personalized asthma management
- Biologic therapies are already being used regularly and will only expand in the future

Questions?

OHSU

Combined Clinic for Severe Sinus Disease

ENT & Allergy

Venous Thromboembolic Disease

Tom DeLoughery, MD MACP FAWM @bloodman
Oregon Health and Sciences University
GENERAL HEMATOLOGY
OHSU

DISCLOSURE

Relevant Financial Relationship(s)

Speaker Bureau - None

Consultant/Research – none

How Long Should DVT patients be at Bedrest?

Is Bedrest Useful in DVT Patients?

- **At eight trials (N= 5700) compared bedrest with activity**
- **No trial showed a difference in PE or thrombosis**
- **One study showed decreased pain and swelling with activity**
- **Management**
  - **Activity: as tolerated**
  - **Trial of elastic stockings knee-high 30-40 mmHg**

Exercise: Key Therapy

- **Less post-thrombotic syndrome in more active patients**
- **Less bleeding in anticoagulated patients**
- **Encourage activity!**

What is the Role of IVC filters in 2020?

Inferior Vena Cava Filters

- Overused and under studied!

Filters

- Only 3 RCT
- No influence on mortality in anticoagulated patients
  - Only one study showed reduction in PE
- ~1-2% fatal PE rate in IVC filters patients in ICU studies
- Raises risk of future DVT (~2x)

Medicare

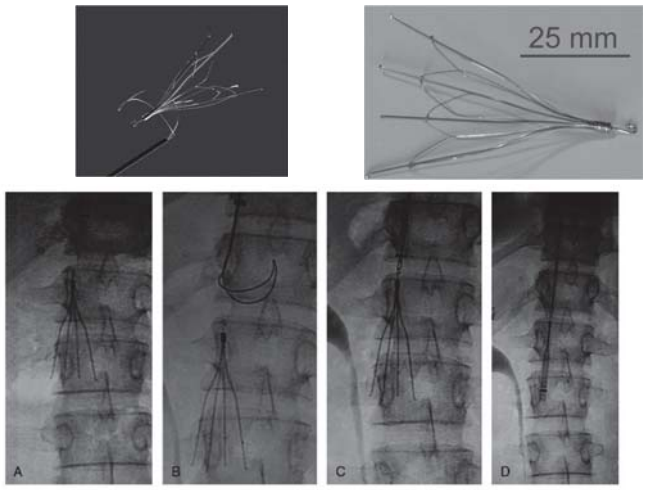
- 13% of Medicare patients with PE received filters
- OR for death 1.35-1.61
  - One year 2.19
- JAMA Intern Med 2019;179(2):263-265

IVC Filters

- Recent cohort study of patients unable to be anticoagulated
- Adjusted for "Immortal time bias"
- HR death = 1.18 (1.13-1.22)
- Need RCT
- JAMA Netw Open 2018;1(3):e180452.

2019 Trauma Trial

- N = 240 trauma patients with contraindication to anticoagulation
- No difference in PE in filter vs no filter group
- N Engl J Med 2019; 381:328-337



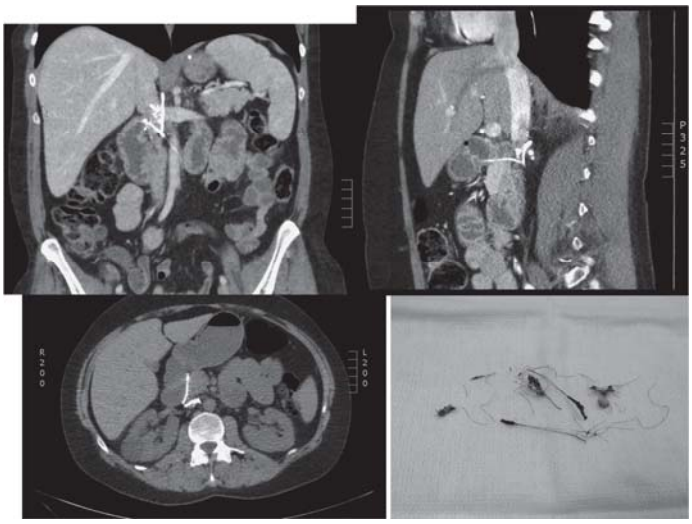
Arch Bronconeumol. 2011;47:17-24

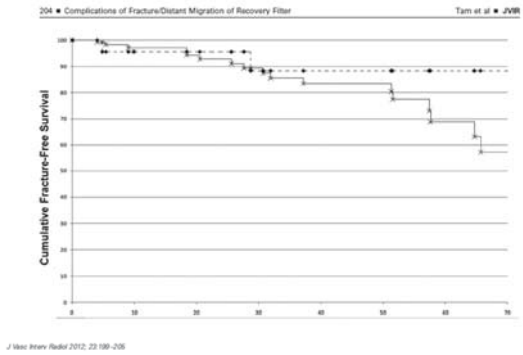
Retrievable Filters: Panacea or Pandemic?

- Rapid acceptance of retrievable filters
- Caveats
  - 10-20% cannot be removed
  - > 50% aren't removed
  - Limited clinical studies
  - Limited long term follow-up

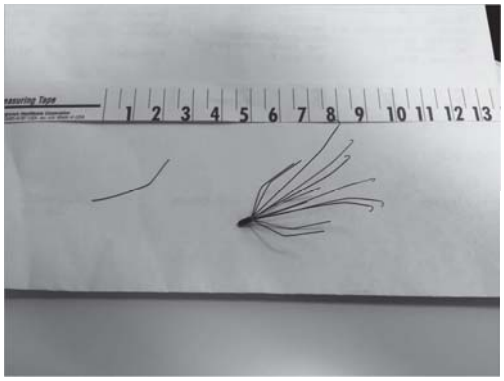
Retrievable Filters

- Need system in place to retrieve
- Reports of retrieval many years out
- Can retrieve while anticoagulated
- Strut factures from non-removed filters increasing issue



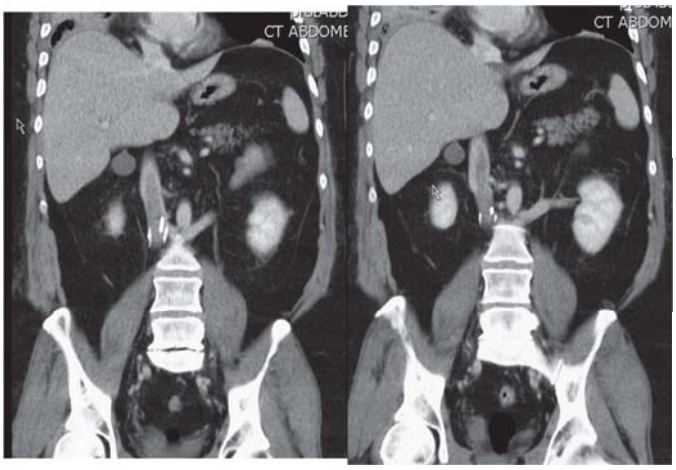


Strut breakage up to 40-50% at five years



IVC Filters

- Still should be used with caution
- Indications
  - Large DVT and temporary contraindication to anticoagulation
  - NOT indicated for PE prophylaxis
- Patients must be warned that "retrievable" filter may be permanent
- Will RAISE the risk of DVT!
- Need to anticoagulate <u>as soon</u> as feasible



Reasons NOT to Put in a Filter

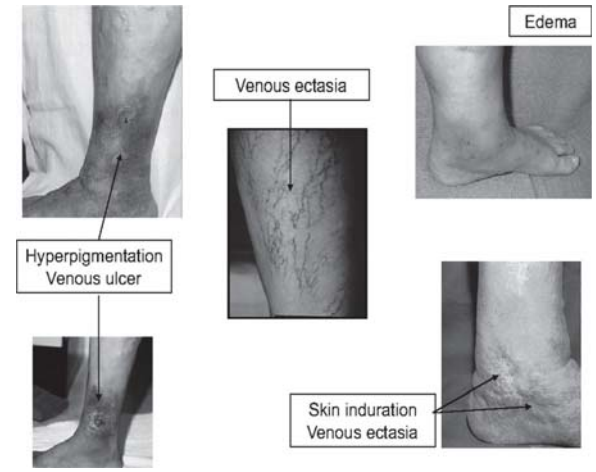
- Pulmonary embolism:
  - 1st week of anticoagulation
  - Despite warfarin
- Deep venous thrombosis:
  - With free floating thrombus
  - Extension of DVT
  - Despite warfarin
  - In cancer patients

Curr Opin Hem 2009 Sep;16(5):402-6

How do we prevent Post-Thrombotic Syndrome?

Post-Thrombotic Syndrome

- Common complication of DVT
- 20-50% of all patients
- 5-10% severe
- Can be disabling



Blood, 19 November 2009, Vol. 114:4624-4631.

PTS: Risk Factors

- Common femoral or iliac vein thrombosis
- Previous DVT
- High BMI
- Older age
- Inadequate initial anticoagulation

Prevention

- Prevent thrombosis!
- Knee-high compression stockings – controversial but…
  - Apply within 24 hours
  - 30-40mmHg
  - At least 6 months
- Keep the patient active
- DOACs
  - 3 studies show less PTS

Therapy of PTS

- Compression stockings
  - Knee high
- Leg elevation
- Horse chestnut seed extract
  - BID for a 12 weeks trial
- Treat neuropathic pain
- Leg massage
- Venous stenting (?)

Post-PE Syndrome?

- 50% of patients with PE report dyspnea 6 months later
- 20-70% state health status worse
- Seemingly not related to clot residual or scarring
- Chest pain/discomfort very common
- Warn/reassure patients
- "Cardiac" rehab

How Long do we treat Venous Clots?

Duration of Therapy

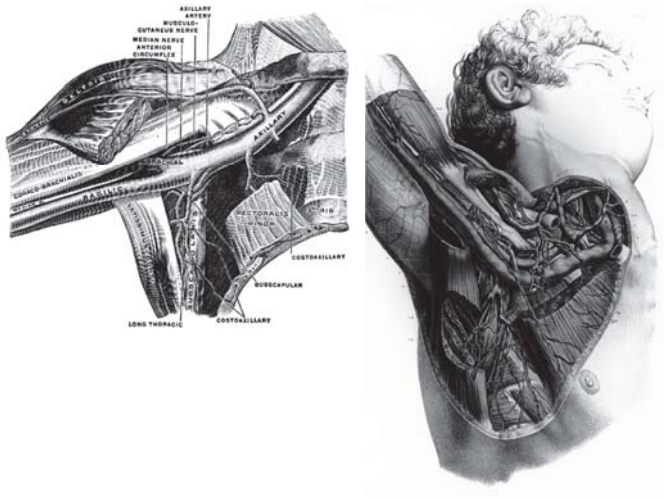
Idiopathic versus provoked thrombosis is <u>the biggest</u> determinant of risk of recurrent thrombosis

Duration of Therapy

- Not all thrombosis are the same
- Can stratify patients by:
  - Site of thrombosis
  - Circumstances of thrombosis
    - Most important!
  - Presence of hypercoagulable states

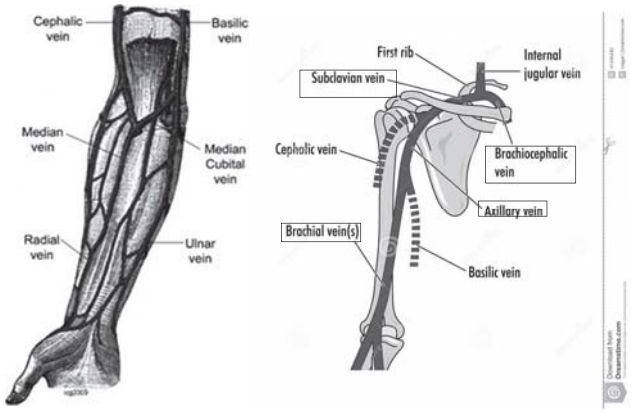
Upper Extremity Thrombosis

- Mechanical defects
  - Catheter
    - PICC 3-5%
  - Local venous trauma
- Prophylaxis ineffective
- Low risk of serious sequela



Upper Extremity Thrombosis

- Therapy: PICC Catheter
  - Key is removing catheter
  - No new one for at least 10 days
  - Benefit of anticoagulation uncertain
    - 25% rate of bleeding
  - Remember many are superficial thrombosis



Upper Extremity Thrombosis

- Therapy: Non-PICC Catheter
  - Line can be removed
    - Assess need for anticoagulation
  - Line cannot be removed
    - 3 months anticoagulation
    - High rates of serious bleeding

Upper Extremity Thrombosis

- "Spontaneous"
  - 3 months anticoagulation
  - Look for underlying vascular defects
  - Consider thrombolytic therapy
    - ~75% with underlying lesions

Portal Vein Thrombosis

- Very common finding
  - With screening for hepatomas
  - After surgery
- Increasing guidance

Portland Portal Vein Protocol

Portal Vein: Cirrhosis

- Incidental
  - SMV negative – no treat
  - SMV involved - treat
- Symptomatic – treat

Noncirrhotics: Symptomatic

- Provoked
  - Surgery
  - Infection, etc.
    - Treatment: 3 months
    - Work-up: not recommended
- Unprovoked
  - PNH, MPS, APLA
  - Indefinite anticoagulation

2017 Meta-Analysis

- 8 studies with 353 patients
- Recanalization
  - 71% vs 42%
- Complete recanalization
  - 53% vs 33%
- PVT progression
  - 9% vs 33%
- Bleeding
  - 11% vs 11%
- Gastro 153:480, 2017

DOAC in PVT

- Increasing data on safety in liver disease
  - Easier to use
  - Less bleeding
- Drug of choice
- Exception Child C
  - Case by case basis

Superficial Thrombophlebitis

- Very common
- Strong inflammatory component
- Wide range of therapeutic options

STP: LMWH

STTEPS

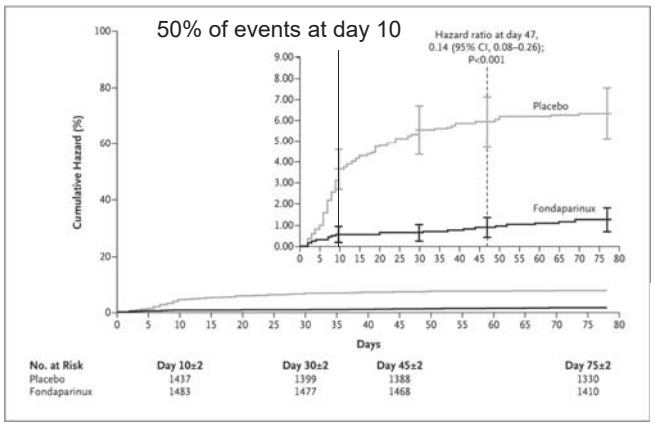
- Symptomatic STP
- 8-12 day of therapy
  - Placebo: 30.6% (3.6%)
  - NSAIA: 14.9% (2.1%)
  - 40 mg LMWH: 8.3% (0.9%)
  - 1.5 mg/kg LMWH: 6.9% (1.0%)

Vesalio Study Group

- Greater saphenous vein STP
- One month of therapy
  - Prophylactic dose: 7.2%
  - Treatment dose: 7.2%

Superficial Thrombophlebitis

- Fondaparinux 2.5 mg/day x 45 days
  - Endpoint: F: 0.9% P: 5.9%
  - DVT/PE F: 0.2% P: 1.5%
  - No difference in bleeding
  - Need to treat 88 patients to prevent one DVT/PE
  - NEJM 363:1222-32, 2010



Decousus H et al. N Engl J Med 2010;363:1222-1232

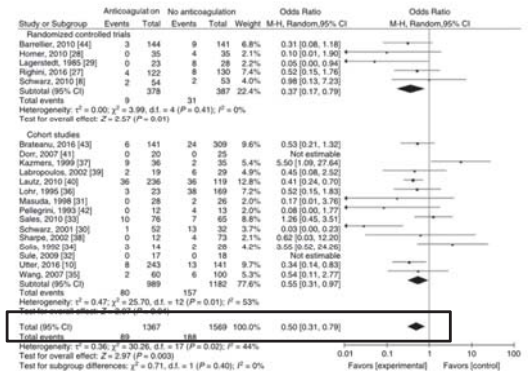
Superficial Thrombophlebitis

- Small and distal: NSAIA and heat
- Painful, large (> 5cm) or greater saphenous vein
  - At least 10 days of prophylactic dose LMWH or fondaparinux
- Role of DOAC uncertain
  - ? DVT rate

Calf Vein Thrombosis

- High risk of progression
  - Up to 10% progression
  - PE rate 2-3%
- 12 weeks therapy for most patients

Calf Vein Thrombosis Therapy



Journal of Thrombosis and Haemostasis, **15**: 1142–1154

Calf Vein Thrombosis Therapy

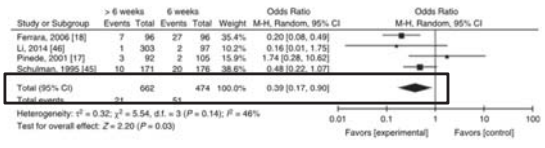


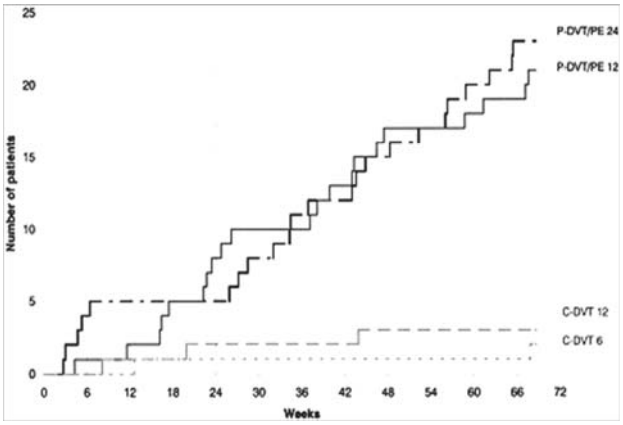
Fig. 6. Recurrent venous thromboembolism in patients receiving anticoagulant treatment for > 6 weeks versus 6 weeks. CI, confidence interval; d.f, degrees of freedom; M-H, Mantel-Haenszel. [Color figure can be viewed at wileyonlinelibrary.com]

Journal of Thrombosis and Haemostasis, **15**: 1142–1154

Duration of Therapy: Proximal DVT

- 3 months
  - Provoked DVT
    - Especially estrogen related
- No benefit with 6 months except more bleeding
- Obtain scan at end of therapy for new baseline
  - J Thromb Haemost. 2011 Dec;9(12):2406-10

Proximal DVT



Circulation, May 2001; 103: 2453 - 2460.

Duration of Therapy

- What is an Idiopathic Thrombosis?
  - No trauma, surgery or hospital stay for 1-3 months
  - No estrogens
  - No long travel
  - Exact definition controversial

1st Idiopathic VTE

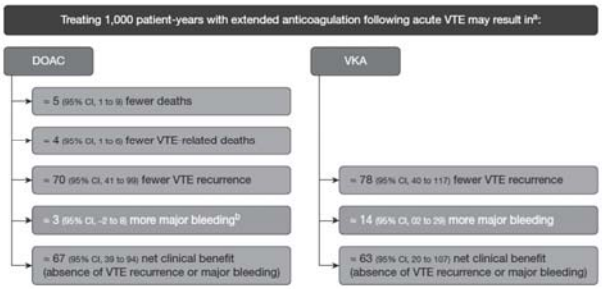
- High rates (30-40%) of recurrence off anticoagulation
- Multiple RCTs show benefit of long term anticoagulation
  - Marked increase in recurrence when stopping anticoagulation

BMJ 2019 Meta-analysis

Year	Risk	Cumulative Incidence
1 Year	10.3%	-
2 year	6.3%	16%
3-5 years	3.8%/year	25% 5 years
6-10 years	3.1/year	36% 10 years

Case fatality rate for recurrence 4%
Distal thrombosis 1/10th of risk
BMJ 2019: 366:4364

Extended Therapy



Chest 2019 in press

D-Dimers

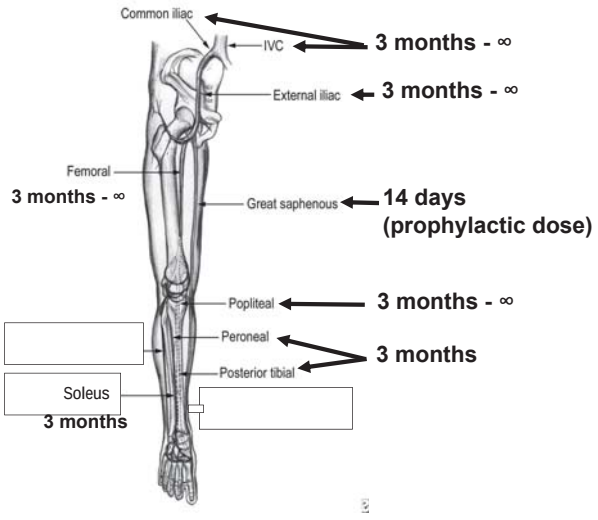
- **D-dimers checked off therapy to predict risk**
- **Meta-analysis**
  - **7 studies**
  - **Positive D-Dimer: 10%/yr**
  - **Negative D-Dimer: 2.9 - 4.0%/yr**
- **Unclear if repeat testing helps**
- **Most recent study showed high rates of recurrence with negative D-dimer 5%/yr**

Idiopathic VTE

- **No good prediction rules**
  - **Negative D-dimer - NOT predictive**
  - **Thrombus resolution – NOT predictive**
- **Still need better prediction rules!**
- **Safer anticoagulants is shifting balance toward longer treatment**

Duration of Therapy

- **Indefinite**
  - **>1 DVT (except upper ext)**
  - **Acquired hypercoagulable states**
  - **Idiopathic unusual site**
  - **Idiopathic severe pulmonary embolism**
- **3 months**
  - **Provoked pulmonary embolism**



What about Hypercoagulable States?

Hypercoagulable State

- Clear risk factor for 1st VTE
- No evidence with classic genetic states predict recurrence
- Multiple guidelines against checking in provoked thrombosis

Thrombophilia Work-Ups

- Don't screen for genetic causes
  - For provoked thrombosis
  - Arterial thrombosis
  - Upper extremity thrombosis
- ~$1200

What Are The Role Of The New Anticoagulants In Venous Thrombosis?

Novel Anticoagulants

- Robust randomized trial data for all new anticoagulants
- Now recommend by ACCP first line over warfarin
- Irreversibility = Myth
  - Less need to reverse
  - No difference in bleeding outcomes in multiple studies

DOAC in VTE

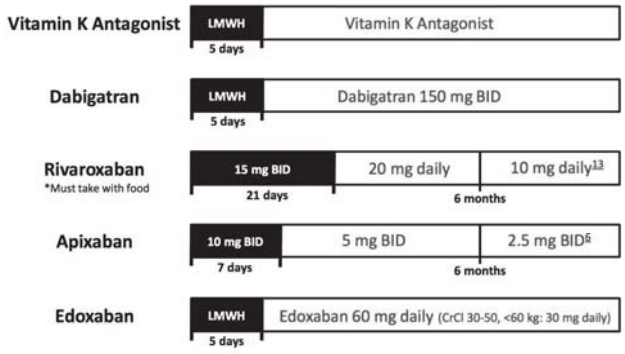
- Recurrent VTE: 0.90 (0.77-1.06)
- Major bleeding: 0.74 (0.59-0.85)
- ICH: 0.37 (0.21-0.68)
- Fatal bleeding: 0.36 (0.15-0.84)

Blood 2014;124(12):1968-1975
Eur J Vasc Endovasc Surg. 2014 Nov;48(5):565-575.

Venous Thrombosis

Drug	Heparin First?	Thrombosis	Bleeding
Apixaban	No*	Equal	Safer
Dabigatran	Yes	Equal	Equal
Edoxaban	Yes	Equal	Safer
Rivaroxaban	No*	Equal	Safer

*Apixaban 10mg bid x 7 days then 5mg BID
*Rivaroxaban 15mg bid x 21 days then 20mg daily



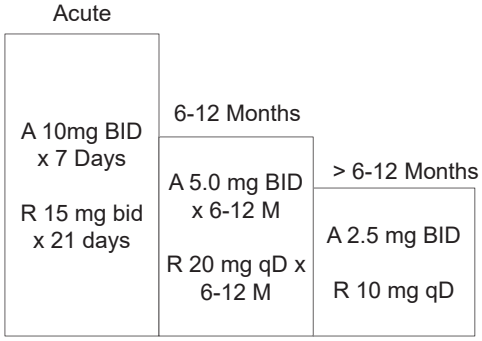
Lower Dose DOACs?

- Older data for lower doses in chronic therapy of VTE
  - LMWH
  - Ximelagatran
  - Did not work for warfarin

Lower Dose Therapy

- Only for chronic venous thrombosis!!
- NOT
  - Atrial fibrillation
  - Cancer
  - Bad thrombophilia
  - Visceral vein thrombosis

DOAC VTE Stepped Care



DOAC in Cancer Patients

- DOAC used in majority of patients
- 3 RCT showing equivalence/superiority with LMWH
  - GI bleeding concern with GI tumors
    - Rivaroxaban/edoxaban
  - Apixaban maybe prefer in patients at risk of GI bleeding
- ASCO Guidelines

Who NOT to use New Anticoagulants

- Dialysis patients
  - Apixaban exception
- Triple positive APLA
- Mechanical Valves
- < 50 or > 150 kg

Direct Oral Anticoagulants

- First line therapy for VTE
- Simplified management
- But
  - Patients still need close follow-up
  - Still need to manage anticoagulants
  - Expense an issue

OREGON HEALTH & SCIENCE UNIVERSITY

Biopsychosocial Approach to Perinatal Mood and Anxiety Disorders (PMADs) 2020 Update

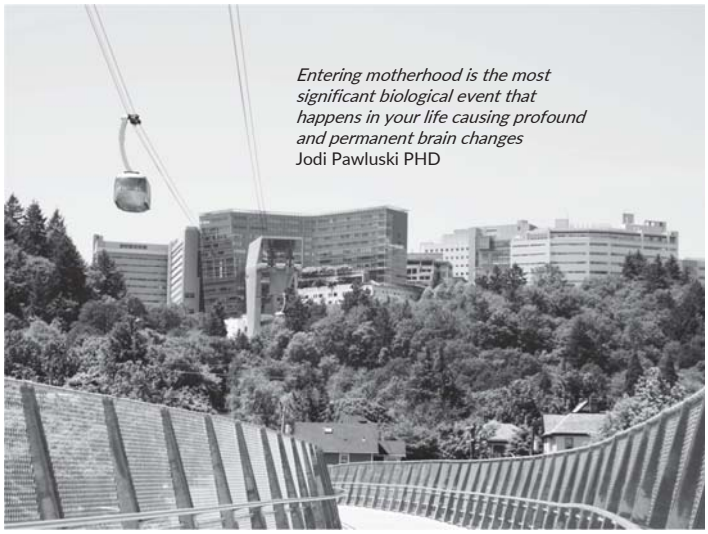
Nicole Cirino MD, Reproductive Psychiatrist
Teni Davoudian, PhD, ABPP
Dept. of Psychiatry and Dept. of OB/GYN
Division of Women's Mental health and Wellness
OHSU Center for Women's Health

Disclosures/Conflict of Interest

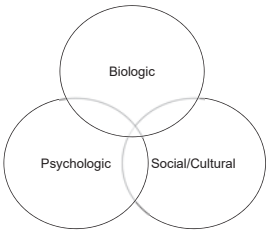
- No COI to disclose

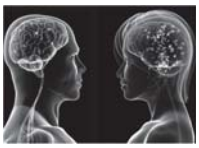
Objectives

- Discuss the role reproductive hormones play in the etiology of PMADs
- Identify screening and monitoring instruments used in identifying PMADs
- Review biopsychosocial risk factors for PMADs
- Summarize the risk and benefit ratio of major classes of psychotropics in the perinatal period
- Identify evidence based behavioral approaches effective in the perinatal period



Male/Female Brain Differences – Neuroplasticity





Neuroplasticity = increased ability to support neural changes, both functionally and structurally

A mother's unique special connection to the child is vital for infants care and survival.

The ability to attach and remain the parent caregiver is the remarkable step that has marked our evolution from reptiles to mammals."

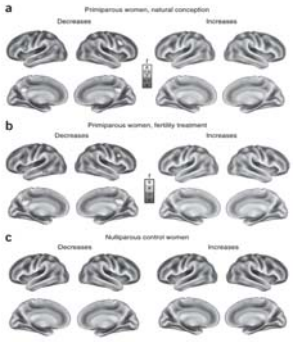
Women's Moods – Deborah Sichel MD

Pregnancy leads to long-lasting changes in human brain structure

Decrease in grey matter assoc. with social cognition

Pruning of glial cells and neurons

Maturation of brain function –fine tuning



Hoekzema et al Nature Neuroscience 2017

A "sensitive period" – Brain changes in motherhood

- Enable a mother to multitask to meet her babies needs
- Emphasize with the infants emotion and pain (and others)
- Decode social stimuli that may equal threat
- Sync her brain with her babies for life
  - Synchronized brain responses
  - Matching responses in gaze, touch and vocalization
- Neuronal plasticity that is also receptive to interventions

Elseline Hoekzema Leiden U, Netherlands 2016

Estrogen – Mood Enhancing Effects

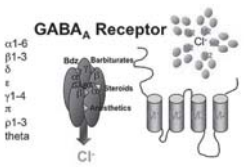
- A 1000 fold increase during pregnancy with rapid drop postpartum
- Estrogen supports Serotonin (5HT)
  - Increases synthesis (tryptophan)
  - Increased 5HT1 receptors in Dorsal Raphe
  - Reduces metabolism of serotonin (Decrease MAO activity)
- Estrogen potentiates Norepinephrine (NE)
- Antidopaminergic effects (DA)

Estrogen – Brain effects

- Facilitates gender specific behaviors in women
  - Interpersonal aptitude
  - Verbal Agility
- Inhibits Fear Response

Progesterone (and Allopregnanolone)

- Elevated in pregnancy with rapid drop postpartum
- Progesterone and allopregnanolone are GABA agonists
- Progesterone can have hypnotic and anxiolytic effects



Oxytocin (OT) and Attachment/Mood

- Fosters attachment b/w all mammalian mothers and infants
- Improves ability to interpret social situations and facilitates attending to others
- OT activates limbic structures assoc. with emotion and *attention –peaks day 3-5 PP*
- Postpartum women: Lactation suppresses physiologic response to stress.
- Promotes amnesia during labor

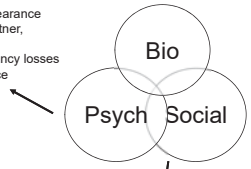
PMADs

- Large spectrum of diagnoses and severities
- Cross socioeconomic, racial, and ethnic lines
- Depressive spectrum:
  - Baby blues
  - Antenatal depression
  - Postpartum depression
- Anxiety spectrum:
  - Generalized anxiety
  - OCD
  - Panic Disorder
  - PTSD
- Postpartum mania/hypomania
- Postpartum psychosis

Etiology of PMADs

Etiology of PMADs

- Exacerbation of underlying psychopathology
- Anxiety about pregnancy & motherhood
- Intergenerational issues
- Depression about physical appearance
- Changing relationships with partner, colleagues, friends
- Grief related to previous pregnancy losses
- Grief about loss of independence



- No paid maternity and/or paternity leave
- Mothers expected to resume total self-care within a few days
- Financial concerns
- Limited social support
- Higher rates of IPV among high-risk populations

***Zuo Yue* -China**
*M*onth-long postpartum recovery to restore the balance of yin (properties of female, dark, cold) and yang (properties of male, bright, hot) within their bodies.

***La Cuarenta*- Mexico**
40-day rest period that includes protective seclusion; proscription from household chores, shopping, and sexual intercourse; and assistance and education from female relatives.

Sam Chul* - *Rural Korea
Thick rope referred to as the fetal line is hung over the doorway of homes to signify that the new mother is in social seclusion.

Implications of Untreated PMADs

Prenatal Care	• Fewer prenatal visits • Inadequate maternal weight gain/poor nutrition • Poor maternal self-care • Possible substance use
Obstetrical Complications	• Intrauterine growth restriction • Miscarriage • Preeclampsia • Preterm labor and birth
Neonatal Outcomes	• Low birth weight • High levels of reactivity • Disorganized sleep patterns • Difficult temperament
Parenting	• Physical and psychological unavailability • Limited sensitivity toward infant's needs • Overly sensitive and reactive parenting (anxiety) • Impaired bonding

PMADs Risk Factors

- Personal/familial mental health history
- History of hormonal sensitivities
- Childhood sexual trauma
- Negative attitude or ambivalence toward pregnancy
- Intimate partner violence
- Limited social support
- Multiparity
- Obstetrical complications
- NICU stay
- Characterological patterns (neuroticism, perfectionism, rigidity)

Assisted Reproduction

- No significant difference in perinatal anxiety and depression in medically assisted conception groups and control groups
- ART aspects that may impact mental health
  - Lower relationship satisfaction due to stressors of ART
  - Multiparity
  - More reproductive traumas?
  - Idealization of parenting?

Breastfeeding

- Increases, decreases, or does not impact risk of PMADs?
- Effects of breastfeeding on maternal depression are heterogeneous
  - Mediated by breastfeeding intentions
  - Early negative breastfeeding experiences associated with depressive sx postpartum
- Referral to lactation consultants
- Compassionate care for mothers who do not desire to or are unable to breastfeed

Perinatal Depression

- 1 in 7 women experience depression during pregnancy and/or postpartum
- Higher rates among:
  - Adolescents
  - Immigrants
  - Low SES
  - Hispanic and African American women

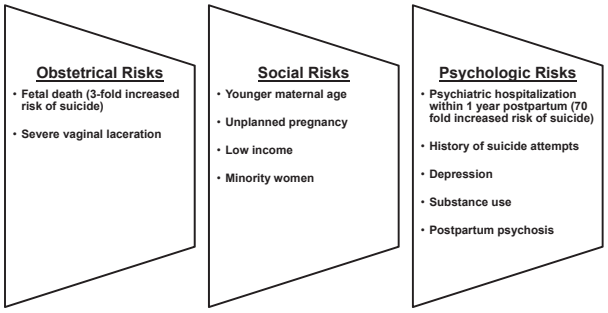
- Screening for perinatal depression, particularly in women of color and women from disadvantaged backgrounds, is imperative!

Baby Blues or Postpartum Depression?

Baby Blues	PP Depression
Rate: 80%	**Rate:** 10-15%
Onset: 3-5 days postpartum	**Onset:** 2 weeks – 6 months postpartum
Course: Transient, taper off by week 2 or 3 postpartum	**Course:** Symptoms persist for at least 2 weeks
Sx: Feeling overwhelmed, uncertain, irritable, mood swings, lonely Mother still able to care for child	**Sx:** Consistent sadness, worthlessness, lowered self-esteem, hopelessness, lack of interest in baby, SI Symptoms interfere with ability to care for self and child
Recovery: With support, rest, and good nutrition, baby blues resolve	**Recovery:** Symptoms persist despite support, rest, and nutrition

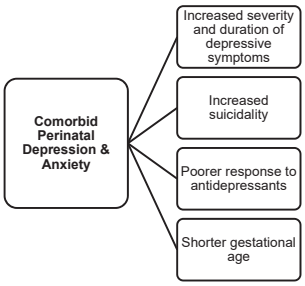
Suicide

- 15% report thoughts of self-harm during pregnancy and postpartum
- Leading cause of death in perinatal women



Perinatal Generalized Anxiety

- 10-15% prevalence in pregnancy and postpartum
- Symptoms
  - Excessive, uncontrollable worry
  - Excessive reassurance seeking
  - Difficulties sleeping when baby sleeps
  - Functional impairment
- High rate of comorbid perinatal depression and anxiety



Physical & Mental Health Postpartum

- Direct correlation between number of physical complaints and intensity of depression postpartum
- Depression and anxiety may contribute to slow recovery
- Common issues:
  - Urinary incontinence
  - Perineal pain
  - Sexual problems
  - Back pain
  - Constipation
  - Breast pain

Perinatal OCD

- 30% new onset
- Peak incidence: 2-4 weeks pp (rapid onset)
- Symptoms:
  - Intrusive, repetitive thoughts and/or images related to baby
  - Ego-dystonic thoughts
  - Checking and avoidance behaviors
- No increased risk of harming infant (unless patient is suicidal)
- Risks: infant neglect, avoidance, attachment disorders
- Thoughts/images ⇄ facts or actions

Perinatal PTSD

- 1 in 10 preterm delivery rate
- 1 in 160 births are stillbirth
- 40% of women report traumatic labor and/or delivery
- Prevalence of PTSD
  - 6 weeks post-partum: 3.1%
  - High risk perinatal population: 16%
  - Following IUFD: 25%
  - Following NICU or PICU death: 35%

Slide adopted from Nicole Cirino, MD and Jacquelyn Knapp, MD

PTSD Symptoms

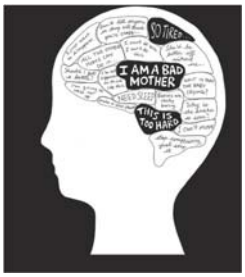
T – Traumatic Exposure	• Direct exposure • Witnessing a trauma • Learning of loved one's trauma • Indirect exposure during professional duties
R – Re-experiencing	• Intrusive thoughts • Nightmares • Flashbacks
A – Arousal	• Hypervigilance • Irritability • Risky/destructive behaviors
U – Unable to function	• Significant distress and functional impairment
M – Month	• Symptoms persist for at least one month
A – Avoidance	• Trauma-related thoughts, feelings, reminders, locations
Negative Affect and/or Cognitions	

Seeking Mental Health Treatment

- Barriers
  - Fear of losing parental rights
  - Expectations to experience joy
  - Normalization of symptoms
  - Socioeconomic issues
  - Limited knowledge of PMADs
    - Misinterpreting symptoms as signs of poor parenting skills
- Facilitators
  - Availability of childcare facilities
  - Flexible treatment options
  - Rapport with referring provider
  - Culturally sensitive care
  - Collocated mental health and ob/gyn care

Psychotherapy Themes

- Evolving roles and identity
- Expectations vs. reality
- Perfectionism and comparison
- Communication breakdowns
- Loss/grief resolution



Perinatal Psychotherapy – Keep it simple!

- Psychoeducational
- Supportive and flexible
- Involve partner and baby in session
- Be directive to patient and partner if needed
- Here and now - not the past
- Supplement with support group(s)

General Psychologic Interventions

- Sleep preservation (important for all PMADs)
  - Poor sleep associated with pp depression and anxiety when controlling for other risk factors
- Widening support network
  - Identify sources of instrumental, emotional, and informational support
- Improve maternal self-care
- Facilitate maternal-infant bond
- Referrals to reproductive psychiatry, faith community, pelvic PT, lactation consultants, doulas, etc

Evidence-Based Psychotherapies

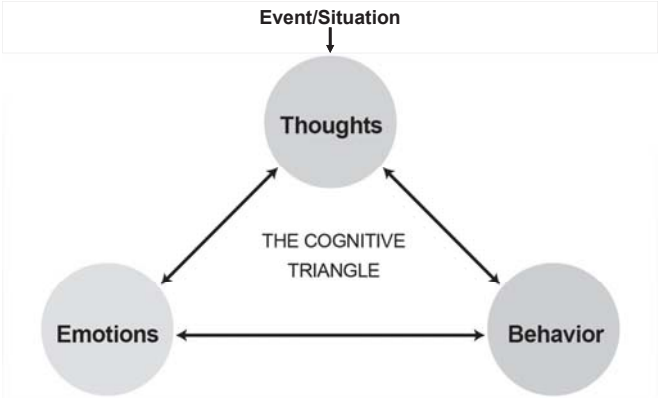
- Individual and group psychotherapy
- Peer support (group or phone)
- Psycho-educational group therapy
- Couples therapy
- Mother-infant therapy and education

- Web-based psych interventions
  - Emerging evidence of effectiveness in treating perinatal depression and anxiety disorders

Evidence-Based Psychotherapies

- Cognitive Behavioral Therapy (CBT)
  - Psychopathology is (partially) the result of faulty information processing
  - Cognitions, emotions, and behaviors are interrelated
  - Cognitions are modifiable

- CBT Goals:
  - Identify and challenge inaccurate, inflated, irrational thoughts or beliefs that distort our perceptions of reality
  - Develop more accurate thoughts and beliefs
  - Cultivate relaxation and coping skills



Cognitive Distortion	Example
Fortune Telling: Predicting that something negative/unwanted will certainly happen (without concrete evidence)	"My baby will have colic."
All-or-Nothing/Black-and-White Thinking: Seeing things as only right or wrong, good or bad, perfect or terrible	"I ate one cookie today so my entire diet is ruined." "Unless I do every single thing that the pediatrician suggests, I'm a bad mom."
Filtering: Focusing only on the negative aspects of a situation and ignoring anything positive or good	"My baby cries all of the time."
Overgeneralization: Thinking that a negative situation is part of a constant cycle of bad things that will always happen. One negative event is seen as a never-ending pattern of defeat.	"I didn't enjoy the first few days of motherhood so I likely won't enjoy being a mom for the rest of my life."
Catastrophizing: Believing that the worst case scenario is the inevitable outcome of a situation and that you will not be able to cope.	"The pain of childbirth is going to be unbearable. I won't be able to manage it."
Personalization: Seeing yourself as the cause of some negative external event	"The baby pushed me away because she doesn't like me"
Should Statements: Telling yourself how you should, ought, or need to act and/or feel.	"I just had a baby. I should be really happy."

Evidence-Based Psychotherapies

- Interpersonal Psychotherapy (IPT)
  - Interpersonal disputes
  - Grief/loss
  - Role transitions

- IPT Goals:
  - Identify maladaptive patterns of communication
  - Learn to communicate needs and emotions
  - Evaluate expectations
  - Explore positive and negative aspects of previous role
  - Develop new attachments

Paternal Depression

- 10% to 25%
- High comorbidity with maternal postpartum depression
- Symptoms: hostility, distancing from others, irritability,
- Contributing factors:
  - Relationship changes
  - Limited sexual intimacy
  - Feeling excluded from mother-infant bonding
  - Hormonal changes? (limited evidence)
- Long-term outcomes of untreated paternal depression:
  - Children with increased risk of conduct problems, hyperactivity, language development

Paternal Anxiety

- Limited research
- Increased anxiety from antenatal period to postpartum
- Contributing Factors:
  - Work-family conflict
  - Partner's anxiety
  - Increased financial concerns
  - Lower education level
  - Lack of understanding of what is expected of fathers
- Negative impact on physical health, social relationships, and paternal self-efficacy

Non-Traditional Families

- Limited research on perinatal mental health of same-sex, transgender individuals, single parents by choice, and gestational carriers
- Stress associated with homophobia, transphobia, and heteronormative medical care

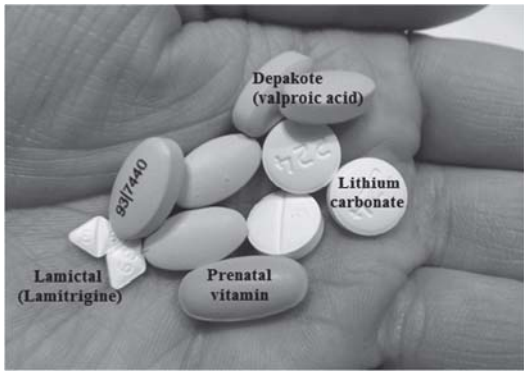
Case – "Mona"

- 35-year-old Hispanic women (G1P1)
- Pregnancy conceived via IUI
- Relocated from Texas to Oregon during pregnancy
- Referred to psychotherapy at 6 week pp visit
  - EPDS=18
- Difficulties breastfeeding
- Feels overwhelmed, irritable, lonely
- Reports intrusive thoughts of harm befalling infant
- Has difficulties sleeping when baby sleeps
- Risk factors?
- Further assessment?
- Interventions/referrals?

Screening and Monitoring Instruments

- EPDS
- GAD-7
- PHQ-9
- CIDI-3

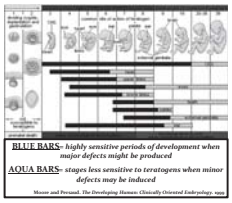
Psychopharmacology in Pregnancy and Lactation



Case - Ellen

27 year old married female with severe Major Depressive Disorder, h/o 2 suicide attempts, 2 hospitalizations presents at 8 weeks GA with acute depression and suicidal ideation after she stopped all meds 2 weeks ago when she found out she was pregnant:

Current meds:
Depakote 500 mg three times a day
Trazodone 200mg at night
Sertraline 150 mg in am
Wellbutrin XL 300 mg at night
Seroquel 50 mg at night 12.5 mg PRN
Clonazepam 0.5 mg at night
H/O ECT -last 18 months ago



Pre-pregnancy Consult

Risk / Benefit = ?

Old FDA Categories(A,B,C,D,X)

Being phased out because misleading

- **A** - No risk in controlled human studies (> 1%).
- **B** - No risk in other studies: often based on animal data only (no human data exists). New medications are labeled B (e.g., lurasidone/Latuda).
- **C** - Risk not ruled out; not necessarily safer than Category D just really no data.
- **D** - Positive evidence of risk; risk known but benefit may outweigh risk (e.g., lithium carbonate).
- **X** - Contraindicated in pregnancy; risk never outweighs benefit (e.g., thalidomide, accutane).

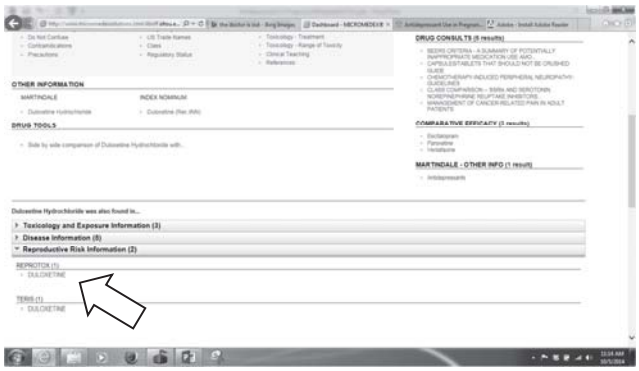
New FDA Categories

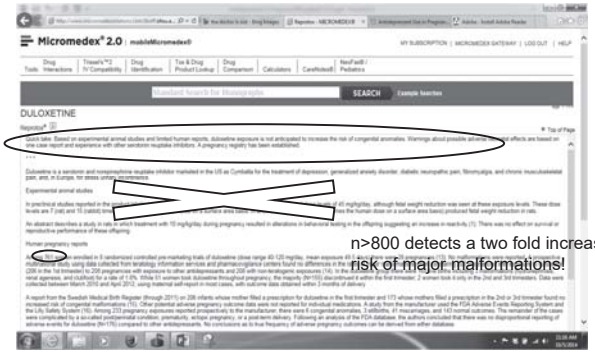
Effective June 30, 2015 **2020 Update**

1. **Pregnancy, Labor, and Delivery**
   - Exposure Registry
   - Risk Summary
   - Clinical considerations
   - Data
2. **Lactation**
   - Risk Summary
   - Clinical consideration
   - Data
3. **Females and Males of Reproductive Potential**
   - Pregnancy testing
   - Contraception
   - Infertility

Resources for Medications in Pregnancy and Breastfeeding

- Reprotox: www.reprotox.org
- Motherisk.org: www.motherisk.org 1-877-439-2744
- www.infantrisk.com ; (806) 352-2519; phone app also available
- Organization of Teratology Information Services: www.mothertobaby.org; good handouts
- MGH Women's Mental Health Program: www.womensmentalhealth.org
- LactMed: www.lactmed.nlm.nih.gov
- E-Lactania: http://www.e-lactancia.org/ingles/inicio.asp
- Tox Net www.toxnet.nlm.nih.gov





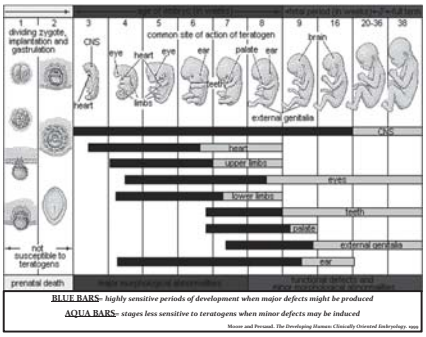
n>800 detects a two fold increased risk of major malformations!

Risks vs. Benefits?

"When a psychiatric condition necessitates pharmacotherapy, the benefits of such therapy far outweigh the potential minimal risks."

(Koren, G., Nordeng, H. Antidepressant use during pregnancy: the benefit-risk ratio. Am J Obstet Gynecol. 2012;207(3):157–63. Epub 2012 Feb 21)

Stages of Human Development – Fetal Age (Gestational age is FA + 2 weeks)



Psychopharmacologic interventions – Medication Classes

- Antidepressants
- Antianxiety/ Hypnotics
- Mood Stabilizers
- Antipsychotics
- Stimulants
- *Brexanolone

TABLE 3
Summary of current knowledge of antidepressant use during pregnancy

Antidepressants likely DO NOT increase the risk of
- Birth defects
- Spontaneous abortion, stillbirth, or neonatal death
- Cognitive impairment or behavioral problems
- Autism

Antidepressants MIGHT increase the risk of
- Late preterm birth (although more likely because of effects of depression)
- Postpartum hemorrhage (although more likely because of other confounders)

Antidepressants likely DO increase the risk of
- Neonatal side effects, especially respiratory distress
- Neonatal persistent pulmonary hypertension of the newborn infant, although rare

Perinatal prescribing pearls
- Ask patients what antidepressant has worked for them in the past and start with this (exception is paroxetine in the 1st trimester).
- One medication at a higher dose is preferable to multiple medications.
- Tapering antidepressants before delivery does not decrease potential fetal risks but does increase risk of symptom relapse postpartum.
- Do not switch effective antidepressants after delivery in lactating women.

Adapted and used with permission from Laura Miller, MD.

Thorness. Perinatal anxiety: diagnosis/management in the obstetric setting. Am J Obstet Gynecol 2018.

Antidepressants- First Line Treatment for Perinatal Anxiety

SSRI	Dosing	Clinical Pearls
Citalopram (Celexa)	Starting dose: 10 mg Range: 20-40+ mg	• EKG above 40mg due to concern over QTC prolongation
Escitalopram (Lexapro)	Starting dose: 5 mg Range: 10-20+ mg	• Not as activating for some patients
Fluoxetine (Prozac/Sarafem)	Starting dose: 10 mg Range: 20-80 mg	• Longest half life • Minimal withdrawal effect if missed dose
Fluvoxamine (Luvox)	Starting dose: 50mg Range: 100-300mg	• Dose at bedtime • Used for OCD • Not indicated for anxiety, panic
Paroxetine (Paxil)	Starting dose: 10 mg Range: 20-40+ mg	• Short half life • Notable withdrawal effects if late/missed dose
Sertraline (Zoloft)	Starting dose: 25 mg Range: 50-200+ mg	• Most commonly prescribed in pregnancy and postpartum • GI distress common at initiation

SNRI (all 2nd line)	Dosing	Clinical Pearls
Desvenlafaxine (Pristiq)	Starting dose: 25 mg Range: 50 or 100 mg	• Very little safety data on use in pregnancy and lactation
Duloxetine (Cymbalta)	Starting dose: 20mg Range: 60-120mg	• Recent increasing amount of safety data on use in pregnancy and lactation • Withdrawal in the neonate
Venlafaxine (Effexor)	Starting dose: 25 mg Range: 75-300 mg	• XR formulation most used • Short half life • Notable withdrawal effects if late/missed dose • Most safety data in pregnancy/lactation of SNRI class

Available Antidepressants and associated Neurotransmitters

SSRIs	SNRIs	Others
Celexa (citalopram) G **Lexapro** (escitalopram) G **Luvox** (fluvoxamine) G **Paxil** (paroxetine) G **Prozac** (fluoxetine) G **Zoloft** (sertraline) G	**Cymbalta** (duloxetine) G **Effexor** (venlafaxine) G	**Wellbutrin** (bupropion) G Bupropion is a weak inhibitor of DA, NE and 5HT reuptake **Remeron** (mirtazapine) G Mirtazapine ↑central noradrenaline and 5HT activity –Anti nausea effects **Brexanolone** GABA-A agonist
Selectively inhibit the reuptake of serotonin (5HT) at the presynaptic neuronal membrane	Inhibit serotonin and norepinephrine reuptake	

G=Generic; B=Brand

Susan: 38 y/o female G1P0 34 weeks GA

"I am very worried about getting Postpartum Anxiety"

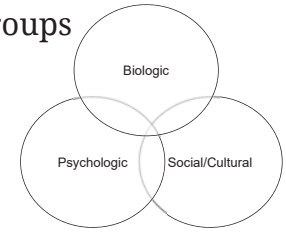
- Past Psych Hx: "Low grade anxiety started at age 13 (social anxiety, fear of flying and one panic attack).
- Fam HX: Sister with obsessive thoughts about earthquake PP.
- SX: Began this pregnancy -Images: Holding her niece and had violent image of dropping infant 2) spilling hot liquid on infant 3) image of her driving off a bridge 4) Panic on recent flight
- ROS: Checking locks at night, has to push door knob several times, has been obsessed with led and led dust
- Last three weeks reports anhedonia, low energy, tearfulness, insomnia
- EPDS 10

$$\frac{\textbf{Risk}}{\textbf{Benefit}} = ?$$

Susan (34 wks) "I am very worried about getting Postpartum Anxiety"

- Psychotherapy - CBT
- Medication – SSRI now, 38 weeks or delivery?
- Perinatal support groups

$$\frac{\textbf{Risk}}{\textbf{Benefit}} = ?$$



Antidepressants and Lactation

- **As a class, antidepressants are considered compatible with breastfeeding and infant exposure is low or negligible.**
- Patients who are successfully treated during pregnancy should not change agents for the purpose of breastfeeding
- **Caution in ill or premature infants.**

Psychopharmacologic interventions – Medication Classes

- Antidepressants
- Antianxiety/ Hypnotics
- Mood Stabilizers
- Antipsychotics
- Stimulants
- *Brexanolone

Benzodiazepines in Pregnancy al JAMA Psychiatry. 2019 May 15.

- BDZ were associated with an increased risk of spontaneous abortion (adjusted OR, 1.85; 95% CI, 1.61-2.12).
- BDZ are not likely strongly assoc. with congenital abnormalities.
- BDZ are assoc. with increased NICU admissions, smaller head circumference (Gen Hosp Psychiatry. 2018)

•Why is this patient taking the medication? Anxiety symptoms? Insomnia? Phobia?
•How is the medication taken? On a daily basis or as needed?
•Is it possible to gradually taper the benzodiazepine?
•If symptoms recur, are non-pharmacologic treatments, such as cognitive-behavioral therapy, effective in this setting?
•If non-pharmacologic options are not successful, could treatment with an SSRI or an SNRI alone be an option?

•WMH.org

Anxiolytics: Benzodiazepines	Dosing	Clinical Pearls
Alprazolam (Xanax)	Starting dose: 0.25mg Range: 0.25 – 2mg	• Only use for acute, discrete panic symptoms on as needed basis • **Most addictive**, short half life • Notable rebound anxiety • AVOID when possible
Clonazepam (Klonopin)	Starting dose: 0.25mg Range: 0.25 – 2mg	• Longest half life • Can use Q12h dosing
Lorazepam (Ativan)	Starting dose: 0.5mg Range: 0.5 – 2mg	• Can dose BID – TID • No active metabolites • Lowest levels in lactation

Anxiolytic (non-benzodiazepine)	Dosing	Clinical Pearls
Buspirone (Buspar)	Starting dose: 5mg Range: 5 – 60mg max/day	• Dosing BID or TID standing (not PRN) • Preferred over benzodiazepine in patient with history of substance abuse/dependence • Not always effective • Minimal data in pregnancy / lactation
Hydroxyzine (Vistaril)	Starting dose: 25mg Range: 25 – 50mg	• Dosing BID – QID • Antihistamine • Frequently used in pregnancy

Sleep Aids	Dosing	Clinical Pearls
Diphenhydramine (Benadryl) Doxylamine (Unisom)	Starting dose: 25mg Range (Benadryl/Unisom): up to 50mg	• Not effective for all patients, especially if anxiety or depression is not fully treated
Trazodone	Starting dose: 25mg Range: 50-200mg	• May cause morning grogginess • Highly effective for many people • No addictive potential • Minimal but reassuring data
Quetiapine (Seroquel)	Starting dose: 12.5mg Range: 25-100+ mg	• Atypical antipsychotic • Low doses effective for insomnia and anxiety • Orthostatic hypotension common first few mornings
Mirtazapine (Remeron)	Starting dose: 7.5mg Range: up to 15mg for sleep	• Inverse relationship between dose and sedation • Used for Insomnia, hyperemesis gravidarum • Stimulates appetite
Zolpidem (Ambien)	Starting dose: 5mg Range: 5-10mg	• Patient may sleep walk • Rapid onset of action • Minimal human pregnancy data

Anna "What's wrong with me, I would do anything for my baby, why can't I do this?"

- 35 y/o female 30 weeks GA with uncontrolled GDM and limited PNC is referred for "anxiety".
- Patient is tearful, **EPDS** is negative, no past psych history.
- She reports when she tries to inject herself with insulin she feels heart racing, dizziness, intense fear. On history she has always avoided doctors "unsure why". Missed several PNVs.

$$\frac{\text{Risk}}{\text{Benefit}} = ?$$

Specific Phobia: Trypanophobia- the fear of needles

- Behavioral therapy – Expos
- PRN lorazepam low dose
- Involve partner and medica[illegible]

$\frac{\text{Risk}}{\text{Benefit}} = ?$

Psychopharmacologic interventions – Medication Classes

- Antidepressants
- Antianxiety/ Hypnotics
- Mood Stabilizers
- Antipsychotics
- Stimulants
- *Brexanolone

Perinatal Bipolar Disorder

- 60% of bipolar women present initially as depressed
- 50% of women with bipolar disorder are first diagnosed in postpartum period
- Up to 85% of bipolar women who go off their medications during pregnancy will have a bipolar relapse before the end of their pregnancy

Perinatal Bipolar Disorder - Pregnancy

Considered to neither protect nor worsen symptoms

- Retrospective review of 101 Bipolar women (after Li discontinuation) showed no difference in pregnant vs. nonpregnant controls for 40 weeks
- Rate of recurrence for 40 weeks was 52%-71% after Li discontinuation
- Higher if discontinuation of LI<14 days.
- 75% risk of relapse after Li discontinuation

Viguera et al, *Am J Psych* 2006

Pregnancy and Bipolar Disorder: Postpartum Period

Postpartum period clearly destabilizes mood

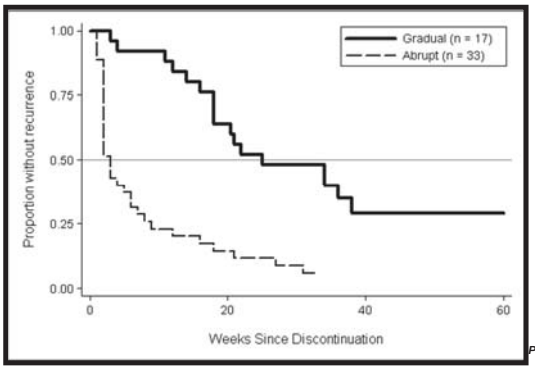
- BP women have 100-fold higher risk than women without a psychiatric illness history of experiencing postpartum psychosis (1)
- 40%-67% of the female BP subject population experienced postpartum mania or depression within 1 month of delivery (2)
- 70 times higher rate of suicide in the first month postpartum

1) Pariser, *Ann Clin Psychiatry* 1993 2) Jefferson et al, 1987

Reproductive Health

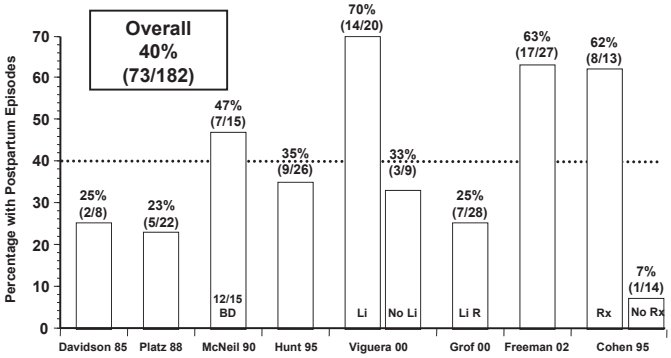
Bipolar Recurrence

Gradual vs. Abrupt Discontinuation



Psych 2006

Postpartum Illness in Women w/ Bipolar D/O



Davidson J, Robertson E. Acta Psychiatrica Scand 1985;71:451-7; Platz C, Kendell R. Br J Psychiatry 1988;153:90-4; McNeil TF in Marneros A, Tsuang M. Affective and Schizoaffective Disorders, Springer, Berlin 1990:72:88; Hunt N, Silverstone T. J Affect Disord 1995;34:101-7; Viguera AC, et al. Am J Psychiatry 2000;157:179-84; Grof P, et al. J Affect Disord 2000;61:31-9; Freeman MP, et al. J Clin Psychiatry 2002; 63:284-7; Cohen LS, et al. Am J Psychiatry 1995;152:1641-5.

Postpartum Relapse Rates

Nonacs, APA 1998

- Euthymic during pregnancy = **27.8%** (n=18)
- Illness during pregnancy = **68.8%** (n=14)

Cohen, Am J Psychiatry 1995

- With Li prophylaxis = **10%** (n=14)
- Without Li prophylaxis = **60%** (n= 13)

The Bipolar Pregnant Patient: Treatment Options

Mild to Moderate Illness

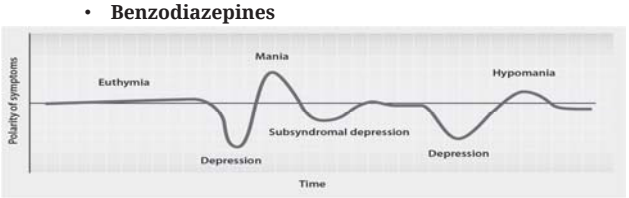
- Trial of safer agent/ monotherapy prior to pregnancy
- Gradual taper of mood stabilizer before pregnancy or when pregnancy test positive
- Maintain drug free in first trimester with low threshold for reintroduction of mood stabilizer

Moderate to Severe Bipolar illness

- Consider continuation of mood stabilizer in first trimester and throughout pregnancy

Bipolar Disorder: Psychopharmacology in Pregnancy

- **Mood Stabilizers**
  - Lithium
  - Antiepileptic Drugs (AED)
    - Valproic Acid (Depakote)
    - Carbamazepine (Tegretol)
    - Lamotrigine (Lamictal)
    - Oxcarbazepine (Trileptal)
- **Antipsychotics**
- **Benzodiazepines**



Perinatal Bipolar Disorder –

Medication	Lithium	Quetiapine (Seroquel)	Lamotrigine (Lamictal)	Clonazepam
Acute Depression	Yes	Yes	Maybe	No
Acute Mania/Hypo	Yes	Yes	No	Yes
Prevention of Depression/Mania	Yes	Maybe	Yes	NO
Onset of action	1-7 days	Hours	4-6 weeks	Hours
Breastfeeding	No	Yes	Yes	Maybe
Known Teratogen	Yes (Ebstein's)	Unknown	Maybe (Cleft palate)	Maybe (cleft palate/lip)
Side Effect Profile	Moderate	Moderate	Mild	Mild
Side Effects	Thyroid, Renal, Tremor, SIADH	SEDATION! Metabolic Syndrome	Rash in 1%	Sedation, Addiction
Maternal Effects	Polyhydramnios	Hyperglycemia	Dose adjustment needed	Withdrawal in newborn
Monitoring	TSH, BUN CR, CBC, Li level, weight	Metabolic labs, Weight	None	None

Anticonvulsants in Pregnancy

Risk of neural tube defects:

- Valproate (1-5%)
- Carbamazepine (0.5-1%)

Valproate (Depakote): Avoid Use!

- Associated with increased risk for adverse cognitive and neurodevelopmental effects compared with other anticonvulsants
- Long-term follow up to 3 years suggests fetal exposure to valproate associated with lower IQ scores (not observed with lamotrigine)

(Khan SJ, et al. Curr Psychiatry Rep (2016) 18:13; Epstein RA, et al. Drug, Healthcare and Patient Safety 2015:7)

Mood Stabilizers in Pregnancy

Lithium: 1st trimester - risk of cardiovascular malformations

- Adjusted risk ratio for cardiac malformations among infants exposed to lithium as compared with unexposed infants was 1.65, *the magnitude of this effect was smaller than had been previously postulated*
- Risk of cardiac malformations appears to be dose dependent
  - RR 1.11 for dose of 600mg or less; 1.6 for dose of 601-900mg, and 3.22 for >900mg

(Epstein RA, et al. Drug, Healthcare and Patient Safety 2015:7 7–29; http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4284049/pdf/dhps-7-007.pdf) Patorno E. et al. N Engl J Med 2017; 376:2245-2254)

Lithium: neonatal side effects

- **Reported side effects:**
  flaccidity, cyanosis, lethargy, hypotonia, poor feeding, abnormal breathing, cardiac arrhythmias, poor myocardial contractility
- Higher Lithium concentrations (in maternal and cord blood) result in more side effects

Simard M et al: Arch Intern Med 149:36-46, 1989; Nishiwaki T et al: Int J Gynaecol Obstet 52:191-21, 1996; Kozma C: Am J Med Genetics 132A: 441-446, 2005; Newport DJ et al: Am J Psychiatry 162:2162-2170, 2005

Lamotrigine in Pregnancy

- Most studies show rates of malformation consistent with general population (Dolk, H. et al. *Neurology* 86.18 (2016): 1716–1725)
- Lamotrigine (Lamictal) exposure carried the lowest risk of overall malformation (Weston J. et al. Cochrane Database Syst Rev. 2016 Nov 7;11)
- No adverse effects of AED exposure via breast milk were observed at age 6 years, consistent with another recent study at age 3 years

(Veiby G, et al. *JAMA Neurol.* 2013;70(11):1367-1374.; Meador et al. *JAMA Pediatr.* 2014;168(8):729-736)

Guidelines for Lamotrigine during Pregnancy

- First Line treatment for Bipolar during pregnancy
- Evidence does not support teratogenesis.
- Increased lamotrigine clearance documented during pregnancy up to 50%.
- Higher doses may be required for clinical response
- 4 mg Folic Acid prior to conception and during pregnancy

Psychopharmacologic interventions – Medication Classes

- Antidepressants
- Antianxiety/ Hypnotics
- Mood Stabilizers
- Antipsychotics → clozapine (Clozaril), risperidone (Risperdal), quetiapine (Seroquel), olanzapine (Zyprexa), ziprasidone (Geodon), aripiprazole (Abilify), asenapine (Saphris), lurasidone (Latuda), paliperidone (Invega)
- Stimulants
- *Brexanolone

Atypical Antipsychotics in Pregnancy

- Quetiapine and olanzapine most studied
- No significant difference in congenital malformations but limited data
- More NICU admissions and c-sections among exposed
- Increased Risk of metabolic syndrome and Gestational Diabetes – consider early nutrition counseling

(Ennis ZN and P Damkier. Basic & Clinical Pharmacology & Toxicology, 2015, 116, 315–320 http://onlinelibrary.wiley.com/doi/10.1111/bcpt.12372/epdf
Sadowsky A. et al. BMJ open access, 2013; http://bmjopen.bmj.com/content/3/7/e003062.abstract)

Antipsychotics in Lactation

- Consider effects of medication on breastfeeding infant and mother
  - EPS, sedation, weight gain
- First generation antipsychotics: small amounts of the drug are excreted into the breast milk: <3% of the maternal dose.
- Second generation antipsychotics: found that <5% of the drug is excreted in the breast milk.

Postpartum Psychosis

- 1 -2 per thousand births (.1- .2%)
- Early onset 90% in the first three weeks
- Medical Emergency
  - –5% infanticide/suicide rate
- Bipolar 7X more likely
- Less than 5% have Schizophrenia

Postpartum Psychoses: Symptoms

- Delusions (e.g. baby is possessed by a demon)
- Hallucinations
- Insomnia
- Confusion/disorientation (more than non-postpartum psychoses)
- Rapid mood swings (more than non-postpartum psychoses)
- Waxing and waning (can appear and feel normal for stretches of time in between psychotic symptoms)

Postpartum Psychosis Treatment

- Hospitalization – Inpatient
- Outpatient Mother-Infant Program
- Around the clock supervision by family member
- Sleep preservation, often D/C BF
- Rule out medical causes
- Antipsychotic Agents
- Mood Stabilizers
  - – Lithium, Anticonvulsants
- ECT
- Inquire About Suicidal / Infanticidal Ideation

High Remission rates in Postpartum Psychosis

64 women with postpartum psychosis using a 4 step algorithm

- Day 1-3 BDZ (*6.3%)
- Day 4-14 Add Atypical AP (*18.8%)
- Day 14 – ADD Lithium (*73.4%)
- After 12 weeks – ECT
- Wean at 9 months

*Remission rates: Total 98.4% acute
79.7% sustained at 9 months.

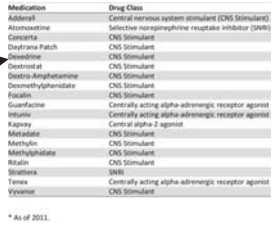
Am J Psychiatry 2015

Postpartum Obsessions vs. Psychosis – Similarities and Differences

Obsessions (OCD or Depression)	Psychosis (Psychotic Disorder)
Intrusive thoughts that cause distress (Ego dystonic)	Aggressive thoughts without guilt or distress (Ego syntonic)
Anxiety, hypervigilance	Confusion, agitation
Fear of acting on or thinking the thoughts	Hearing voices or seeing things that other people don't see
Avoidance or rituals	Bizarre or violent behavior
Personal or family history of anxiety	Personal or Family history of Bipolar
No history of violence, over controlled	History of violence, impulsivity
Rapid Onset of Symptoms	Rapid Onset of Symptoms
Peak incidence 2-4 weeks PP	Peek incidence first 3 weeks PP
May screen negative for depression	May screen negative for depression

Psychopharmacologic interventions – Medication Classes

- Antidepressants
- Antianxiety/ Hypnotics
- Mood Stabilizers
- Antipsychotics
- Stimulants
- *Brexanolone



Medication	Drug Class
Adderall	Central nervous system stimulant (CNS Stimulant)
Atomoxetine	Selective norepinephrine reuptake inhibitor (SNRI)
Concerta	CNS Stimulant
Daytrana Patch	CNS Stimulant
Dexedrine	CNS Stimulant
Dextrostat	CNS Stimulant
Dextro-Amphetamine	CNS Stimulant
Dexmethylphenidate	CNS Stimulant
Focalin	CNS Stimulant
Guanfacine	Centrally acting alpha-adrenergic receptor agonist
Intuniv	Centrally acting alpha-adrenergic receptor agonist
Kapvay	Central alpha-2 agonist
Metadate	CNS Stimulant
Methylin	CNS Stimulant
Methylphidate	CNS Stimulant
Ritalin	CNS Stimulant
Strattera	SNRI
Tenex	Centrally acting alpha-adrenergic receptor agonist
Vyvanse	CNS Stimulant

* As of 2011.

$$\frac{\textbf{Risk}}{\textbf{Benefit}} = ?$$

Psychostimulants in 2020 – A Unique R/B ratio

- Stimulant use on the rise in reproductive-age women age 15-44
  2003= 0.9%
  2015= 4.0%
- Limited data
  - No evidence *thus far* of teratogenesis: methylphenidate and amphetamine agents
  - Associated with growth restriction, low APGAR, stimulant withdrawal syndrome, miscarriage
- No long term neurobehavioral data

Perinatal Psychostimulant Pearls

- Consider stopping stimulants in women with mild or moderate ADHD
  - ✓ Behavioral interventions
  - ✓ Work / home accommodations
  - ✓ Alternate medications (bupropion)
- Dosing: Stay with lowest, studied doses:
  Methylphenidate 15 to 80 mg
  Amphetamine 20 to 35mg
- Immediate Release versus Sustained Release Preparations
  - In lactation – short acting blood levels peak in 1-2 hours – BF or pump right before dosing medication.

Psychopharmacologic interventions – Medication Classes

- Antidepressants
- Antianxiety/ Hypnotics
- Mood Stabilizers
- Antipsychotics
- Stimulants
- *Brexanolone ⟶

Brexanolone 3/19 FDA approved

2012 Update

New medication for moderate to sever postpartum depression

- An allosteric modulator of GABA-A receptors
- 3 days inpatient IV infusion
- Remission of depression often within 24 hours up to 30 days
- SE: Sedation effects ranged from somnolence to loss of consciousness. All resolved within 60 minutes of infusion discontinuation.
- Breastfeeding –12 women/infant dyads. Relative infant dose 1-2%.

1. Kanes SJ, et al. Hum Psychopharmacol. 2017 Mar;32(2)
2. 1. Hoffmann E, Wald J, Colquhoun H. Evaluation of breast milk concentrations following brexanolone to administration to healthy lactating women. Am J Obstet Gynecol. 2019;220:S554. Abstract. DOI: doi:10.1016/j.ajog.2018.11.875
3. Hoffmann E, Wald J, Deng D-H et al. Brexanolone injection administration to lactating women: Breast milk allopregnanolone levels. Obstet Gynecol. 2019;133 (Suppl 1):115S. Abstract 30J. doi:10.1097/01.AOG.0000558846.15461.70 DOI: 10.1097/01.AOG.0000558846.15461.70

Brexanolone 1 year later - Barriers to care
Who, Where, How Much, When?

FDA requires REMS Registration

Who is the right patient for BRX?
DSM-IV or DSM-5
First Line? Second Line?

Sleep Preservation in the Perinatal Period

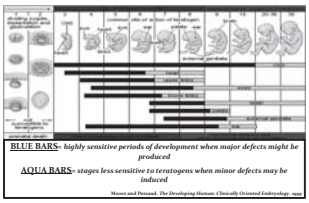
- Loss of sleep leads to depression and psychosis
  - http://www.journalsleep.org/ViewAbstract.aspx?pid=29307
  - https://www.elsevier.com/books/sleep-and-affect/babson/978-0-12-417188-6
  - http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2802254/pdf/aasm.33.1.97.pdf
- Sleep Preservation is an important strategy for all PMADs
- Treat insomnia!
- Introduce one bottle a day
- Night shifts with partner
- Devices (Snoo), books, doulas

2020 Update

Case - Ellen

27 year old married female teacher history of severe Major Depressive Disorder, h/o 2 suicide attempts, 2 hospitalizations presents at 8 weeks GA with acute depression and Suicidal Ideation after she stopped all meds 2 weeks ago when she found out she was pregnant

Current meds:
Depakote 500 mg three times a day
Trazodone 200mg at night
Sertraline 150 mg in am
Wellbutrin XL 300 mg at night
Seroquel 50 mg at night 12.5 mg PRN
Clonazepam 0.5 mg at night
H/O ECT -last 18 months ago



Resources

- **Postpartum Support International**
  - Psychologic and psychiatric support
- **Postpartum Husbands and Dads**
  - **http://www.postpartumdads.org/**
  - **http://www.postpartummen.com/**
- **Massachusetts General Hospital**
  - **http://womensmentalhealth.org/**
  - Info for patients and providers
- **BOOKS**
  - **Beyond the Blues: A Guide to Understanding and Treating Prenatal and Postpartum Depression b** by Shoshana S. Bennett, Ph.D. and Pec Indman, Ed.D, MFT
  - **This Isn't What I Expected: Overcoming Postpartum Depression** by Karen Kleiman, LCSW, and Valerie Raskin, MD
  - **The pregnancy & Postpartum Anxiety Workbook Cognitive Behavioral Therapy for Perinatal Distress** by Pamela Wiegartz, PhD, and Kevin Gyoerkoe, PsyD
  - **Cognitive Behavioral Therapy for Perinatal Distress** by Amy Wenzel, PhD
  - **Token of Affection: Reclaiming Your Marriage After Postpartum Depression** by Karen Kleiman, LCSW

Thank You

Radiographic Findings Associated with Aging: Normal or Abnormal?

❖Barry G. Hansford, MD
❖Oregon Health & Science University
❖Assistant Professor Radiology
❖Musculoskeletal Radiology Fellowship Director

OHSU

Osteoporosis: Terminology

Osteopenia: Paucity of bone, increased radiolucency, descriptive term w/out causality

Osteoporosis: Bone loss/decreased density, normal quality, decreased quantity

Osteomalacia: Malformed bone

Why Is Osteopenia Preferred?
- Cannot tell cause of osteoporosis radiographically
- Cannot discern osteoporosis from osteomalacia
- Generic term encompassing both osteoporosis and osteomalacia

Primary Osteoporosis: Most common in post-menopausal females, osteoporosis of aging

Secondary Osteoporosis: Implies underlying disorder, broad DDX, only 5% of cases

Osteoporosis: Definition

World Health Organization: Bone mineral density 2.5 or more standard deviations less than that of a young healthy adult

T Score: -2.5 SD or less as measured with dual energy x ray absorptiometry (DEXA scan) for post menopausal women and men over 50

Z Score: Abnormal if 2 SD away from mean for age and sex matched norm, relative quantity

Clinical Utility: T score more useful for predicting fracture risk, absolute quantity

Women: Estrogen deficiency after menopause, accelerated cancellous bone loss

Men: More linear pattern of bone loss

Equivalent loss by 80 years of age

Osteoporosis: Morbidity

Common, diminished, but otherwise normal bone

Etiology: Inadequate bone formation or resorption exceeds bone formation

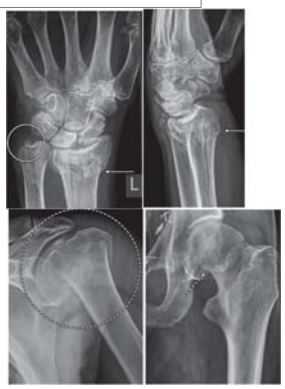
May be localized (disuse) or generalized

Frequency: 13-18% women older than 50, 1-4% men older than 50

Who Cares?
Significant morbidity and mortality, 9 million fxrs year

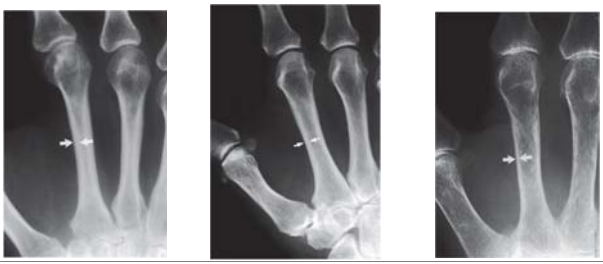
1/3 women and 1/5 men older than 50

Most Common Locations: Forearm, hip and spine



RadioGraphics 2016; 36:1871–1887

Osteoporosis



Radiography:
- Second metacarpal at mid-diaphysis normal cortical thickening should be approximately 1/3 to 1/4 thickness of the metacarpal
- Decreased in osteoporosis

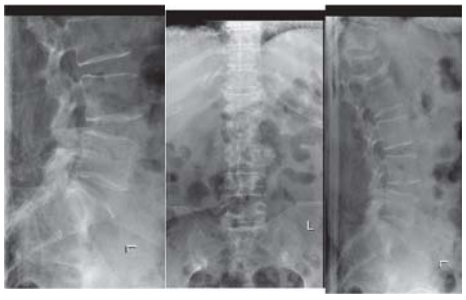
RadioGraphics 2016; 36:1871–1887

Osteoporosis

Radiography
- Thinned cortices
- Endosteal resorption
- Decreased trabeculae
- Intracortical tunneling
- Subperiosteal resorption

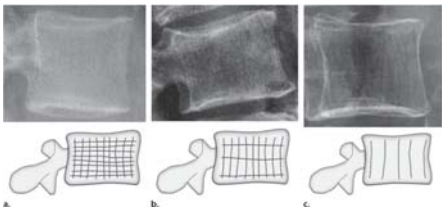
Must have 30-50% bone loss to detect pathology

Picture frame or empty box appearance of vertebral bodies



RadioGraphics 2016; 36:1871–1887

Osteoporosis: Morbidity



Vertebral Bodies: Weight-bearing bones with little cortical bone
- Vertical trabeculae thicker
- Horizontal trabeculae thinner, preferentially lost earlier in disease

History of osteoporotic vertebral body fracture
- Increases risk of future vertebral body fracture X5, 50% asymptomatic
- Increases risk of future hip fracture X2

RadioGraphics 2016; 36:1871–1887

Insufficiency Fractures

Who: Typically > 60 y/o, post-menopausal women

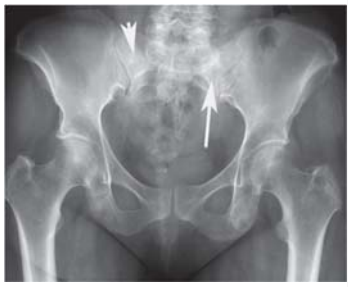
Definition: Abnormal bone under normal stress

Location: Pelvis, sacrum, proximal femur, thoracolumbar vertebral bodies

Presentation: Acute pain, 25% multiple sites, no history of trauma/low impact trauma

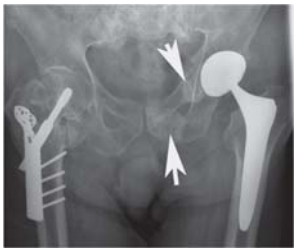
Management: Conservative, bed rest, reduced weight-bearing, simple analgesics

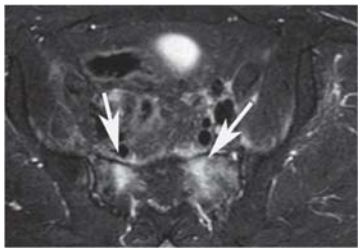
Bisphosphonates: Bone protective therapy, rarely may develop atypical femur fractures



European Journal of Radiology 71 (2009) 398–405

Insufficiency Fractures





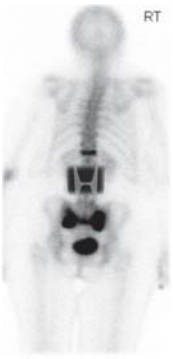
<u>Radiography insensitive but should be obtained first, MRI far superior for marrow</u>

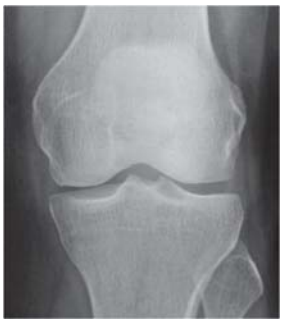
Pelvis/Sacrum: H-shaped Honda or butterfly pattern, pubic bones and acetabulum

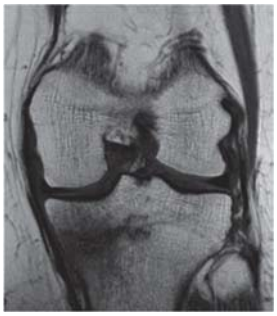
Radiation Therapy: Increases risk

European Journal of Radiology 71 (2009) 398–405

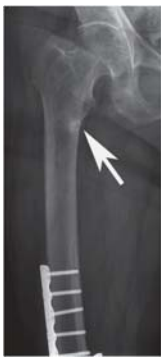
Insufficiency Fractures

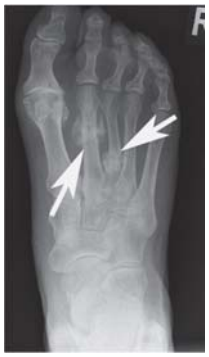


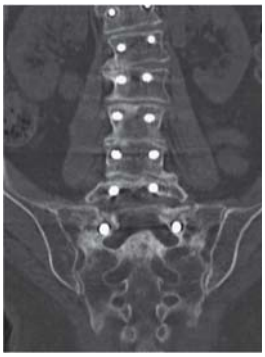




Insufficiency Fractures







European Journal of Radiology 71 (2009) 398–405

Atypical Femoral Fractures

Who: Strong association w/bisphosphonates, increases w/duration of use, must discontinue

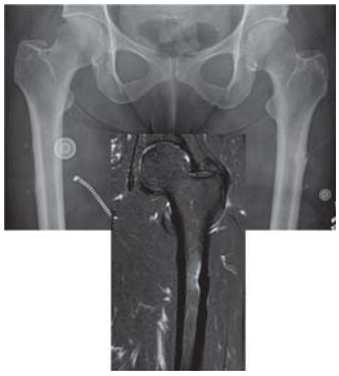
Presentation: May be little to no pain

Location: Subtrochanteric lateral femoral cortex, 50% bilateral must image contralateral femur

Management: If symptomatic, may be surgical

Imaging: Radiography first, if no intracortical fracture lucency, cross-sectional imaging for further evaluation

Radsource: Atypical Femoral Fractures



Osteoarthritis

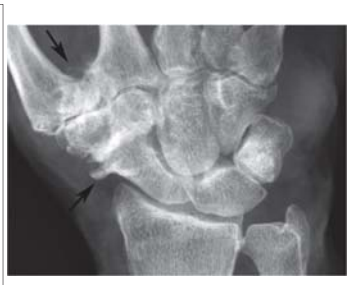
Most common joint disorder

Etiology: Primary/idiopathic, post-traumatic, metabolic bone disease, endocrine disorders

Frequency: > 50% over 65 y/o and > 80% over 75 y/o have radiographic evidence

<u>Symptoms matter! Not radiographic findings in isolation</u>

Imaging Work-up: Always start with radiographs, little to no role for MRI



Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Osteoarthritis

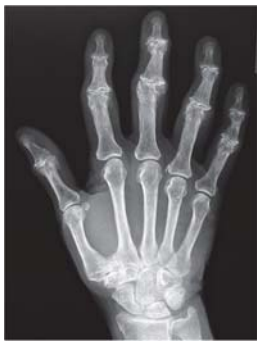
Radiographic Findings:

- ***<u>Osteophyte formation</u>***
- ***<u>Non-uniform joint space loss</u>***
- Normal mineralization
- No erosions
- Subchondral new bone formation
- Cysts
- Subluxations
- Unilateral or bilateral asymmetrical distribution

Locations:

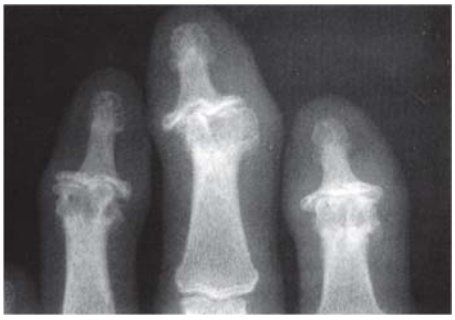
Hands, feet, knees and hips

Spares shoulder and elbows

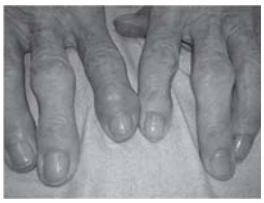


Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Osteoarthritis



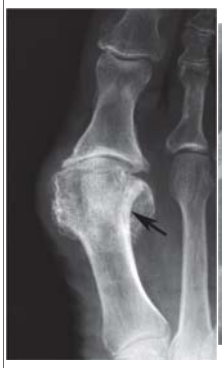
Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

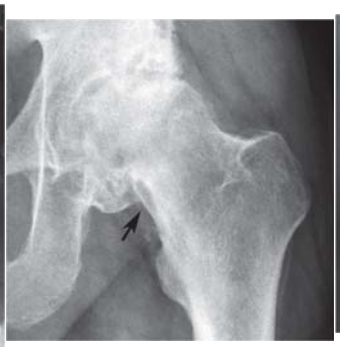


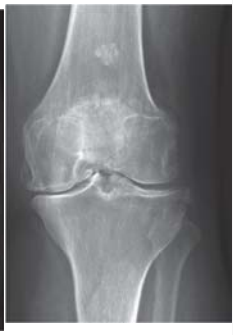
Herberden node:

Osteophytosis and soft tissue swelling

Osteoarthritis

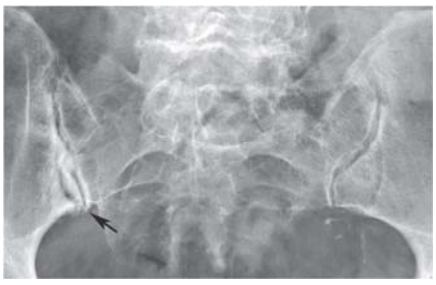


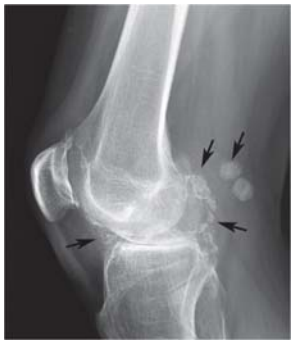




Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Osteoarthritis





Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Imaging of the Shoulder

<u>Radiography should always be obtained first</u>

MRI: Reserved for normal radiographs and persistent pain despite conservative management

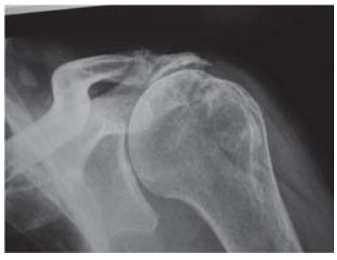
US: Reserved for normal radiographs and persistent pain despite conservative management

CT: Reserved for trauma cases or evaluating bone stock

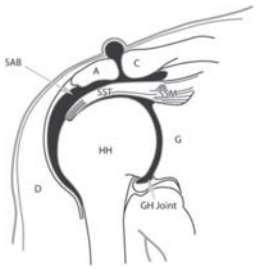
<u>MRI may muddy water and not change management</u>

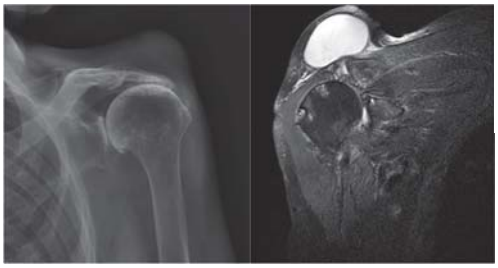
Labral tear/degeneration very common > 40 y/o

Rotator cuff tears may be symptomatic, especially in aging population

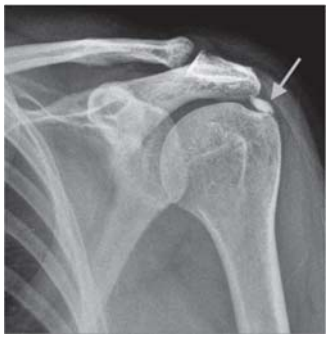


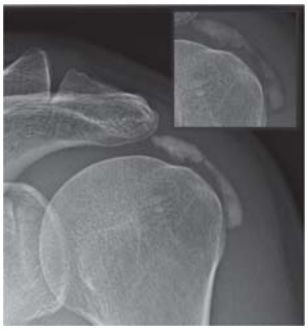
Imaging of the Shoulder





Imaging of the Shoulder





Imaging of the Knee

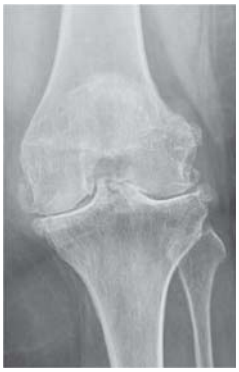
<u>Radiography should always be obtained first</u>

MRI: Reserved for normal radiographs and persistent pain despite conservative management

CT: Reserved for trauma cases or evaluating bone stock

<u>MRI may muddy water and not change management</u>

Meniscal tears may be asymptomatic and surgical treatment may precipitate osteoarthritis



Crystal Disease: Gout

Increasing frequency with aging, 20x M>F

Etiology: Monosodium urate deposition, primary and secondary

Presentation: Hot, painful, swollen joint, can mimic infection

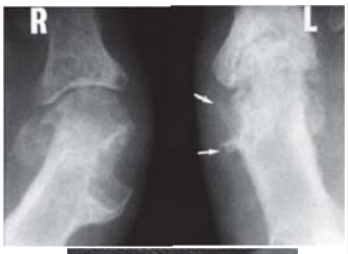
<u>Radiographic findings depend on location of crystals</u>

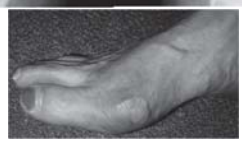
Only 45% of patients have radiographic findings, takes 6-8 years

Cartilage: Osteoarthritis

Soft Tissues: Tophaceous gout

Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition





Crystal Disease: Gout

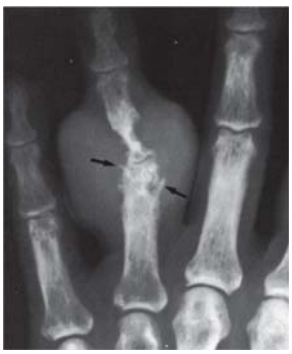
Radiographic Findings:

- Tophi
- Normal mineralization
- Joint spaces preserved
- Punched out erosions w/sclerotic borders
- Overhanging edges
- Asymmetric polyarticular

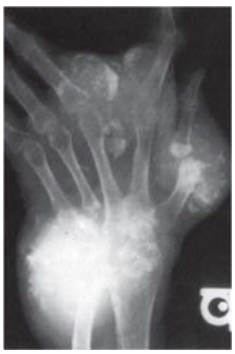
Locations:

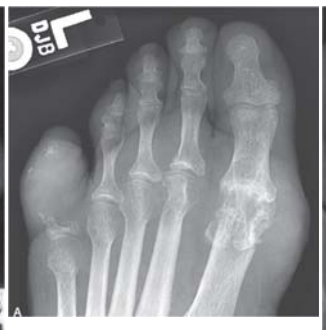
Feet, ankles, knees, hands and elbows

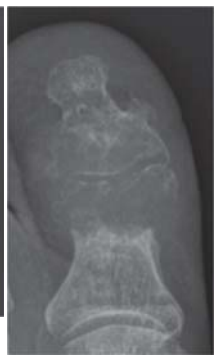
Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition



Crystal Disease: Gout

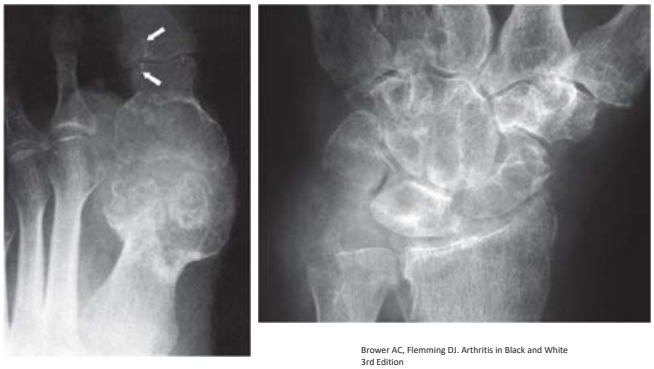






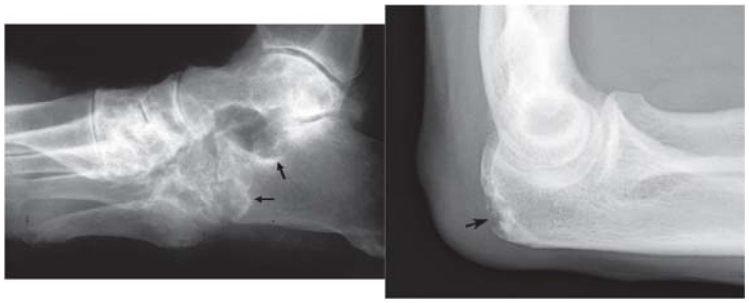
Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Crystal Disease: Gout



Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Crystal Disease: Gout



Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Crystal Disease: Calcium Pyrophosphate Deposition Disease

Most common crystal arthropathy, middle age to elderly

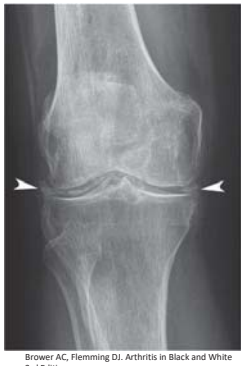
Etiology: Chondrocalcinosis deposition in cartilage

Frequency: Up to 5% of population

<u>Variable presentation and radiographic appearance</u>

Most Common Locations: Knee, pubic symphysis and wrist

Appears similar to osteoarthritis in atypical distribution

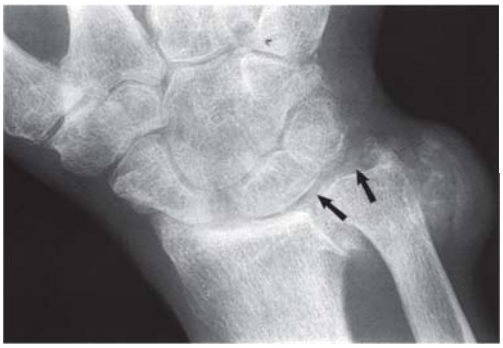


Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Crystal Disease: Calcium Pyrophosphate Deposition Disease

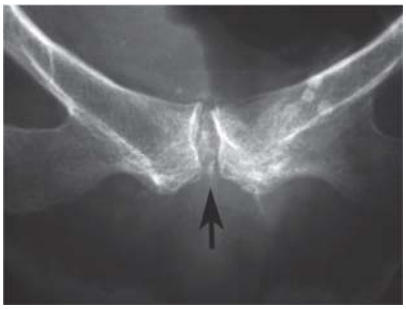
Radiographic Findings:

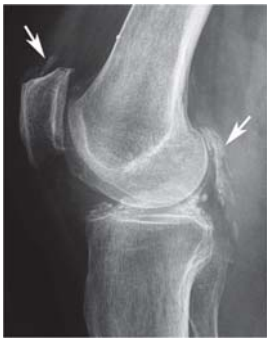
- Chondrocalcinosis
- Normal mineralization
- Uniform joint space loss
- Variable osteophytosis
- Prominent cysts
- Neuropathic rare
- Bilateral
- Involves shoulders and elbows



Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

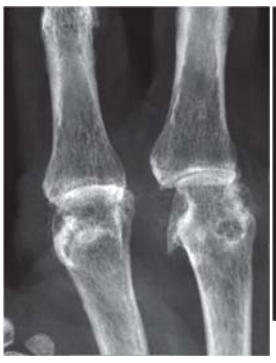
Crystal Disease: Calcium Pyrophosphate Deposition Disease

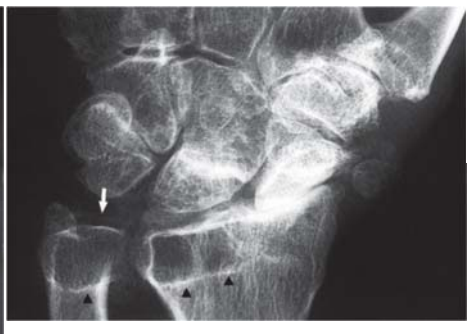




Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

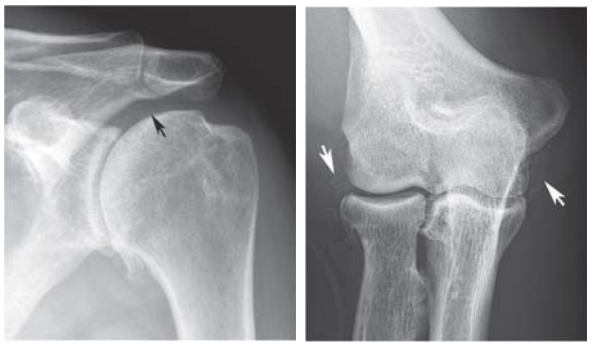
Crystal Disease: Calcium Pyrophosphate Deposition Disease





Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Crystal Disease: Calcium Pyrophosphate Deposition Disease



Brower AC, Flemming DJ. Arthritis in Black and White 3rd Edition

Sarcopenia

Significant muscle loss, a/w cachexia and fragility

Who Cares? Predicator of quality and quantity of life

Particularly in elderly, cancer patients or surgery

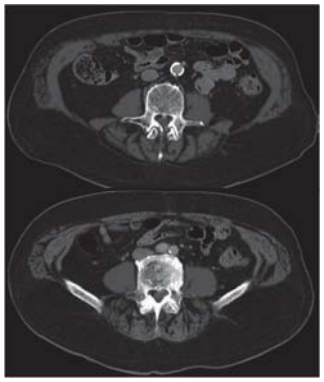
Associations: Physical disability, osteoporosis, falls, prolonged hospital stay, readmission, post-op complications and death

<u>May be Accompanied by Obesity</u>

Imaging CT: May be used as a biomarker of patients already undergoing scan

Use to quantify surface area and density

AJR:205, September 2015



Sarcopenia

Emerging Clinical Applications: Progressive sarcopenia after diagnosis of colorectal cancer has significant negative prognostic association with overall and progression free survival

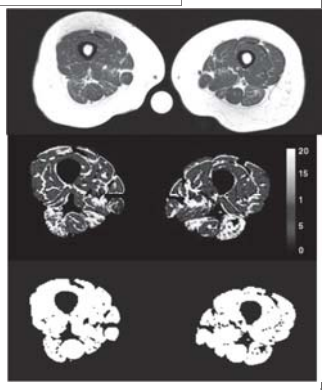
Imaging MRI: Multiple evolving techniques

Future Directions: Best techniques and applications still uncertain

Take Home Points: Independent risk factor for adverse health outcomes

Muscle routinely included on standard cross-sectional imaging

Potentially valuable biomarker AJR:205, September 2015



Metastases and Multiple Myeloma

Patients > 40 y/o with osteolytic lesion without sclerotic borders = Metastases and multiple myeloma

Big Four: Metastases, multiple myeloma, lymphoma and leukemia > 99% of bone cancer

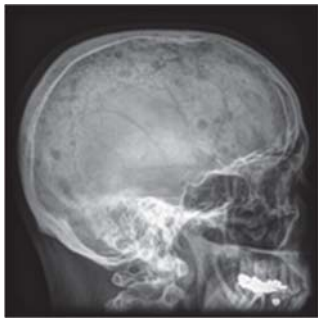
Breast, lung, prostate, kidney, thyroid = 85% metastases

Multiple Myeloma: Most common primary bone malignancy

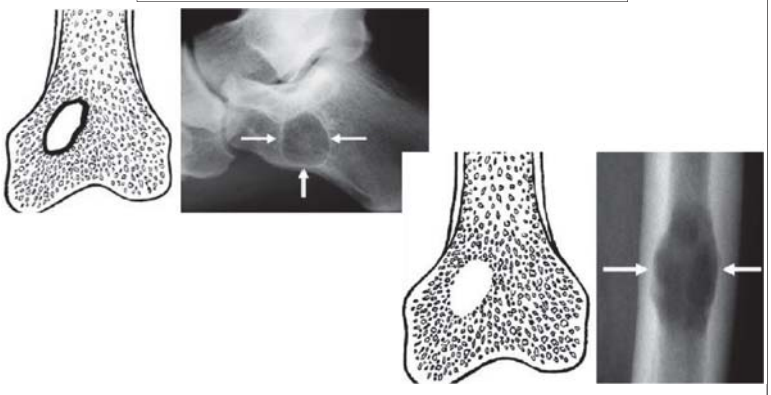
Monoclonal proliferation of plasma cells

Imaging: Punched out lytic lesions of axial skeleton

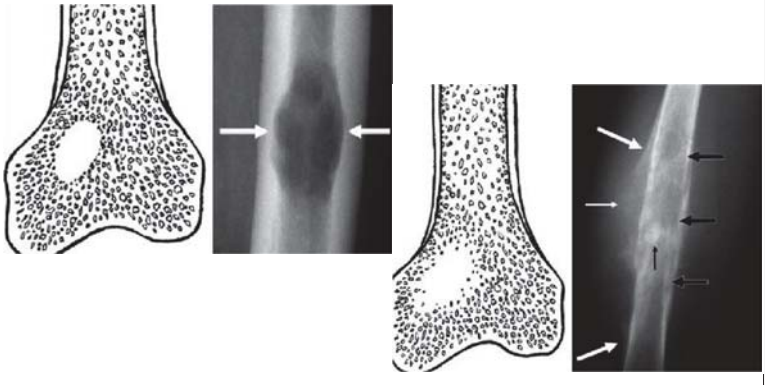
MRI, PET/CT, CT more sensitive



Metastases and Multiple Myeloma

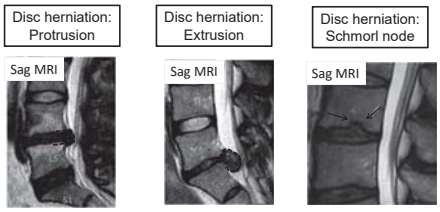


Metastases and Multiple Myeloma



Questions

Radiographic Findings Associated with Aging: Normal or Abnormal?



Dave Pettersson, MD
Assistant Professor of Neuroradiology
Oregon Health & Science University

51st Annual Primary Care Review
February 12, 2020

OHSU

Spine Imaging and Aging:

Disclosures:

Nothing to disclose

Outline:

Spine degenerative changes on imaging:
- Prevalence
- Appearance on MRI, CT, radiographs

Low back pain
- When to image
- "Red flag" conditions

Age-related changes on brain MRI

Spine Imaging and Aging: Question

What percentage of asymptomatic 20-year-olds have degenerative disc findings on lumbar spine MRI?

A. 5 %
B. 15 %
C. 25 %
D. 35 %
E. 45%

Spine Imaging and Aging: Question

What percentage of asymptomatic 80-year-olds have degenerative disc findings on lumbar spine MRI?

A. 35 %
B. 55 %
C. 75 %
D. 95%

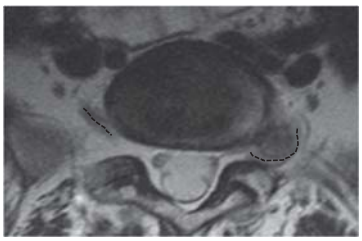
Spine Imaging and Aging: Answers

Systematic Literature Review of Imaging Features of Spinal Degeneration in Asymptomatic Populations

	Age (yr)						
Imaging Finding	**20**	**30**	**40**	**50**	**60**	**70**	**80**
Disk degeneration	37%	52%	68%	80%	88%	93%	96%
Disk signal loss	17%	33%	54%	73%	86%	94%	97%
Disk height loss	24%	34%	45%	56%	67%	76%	84%
Disk bulge	30%	40%	50%	60%	69%	77%	84%
Disk protrusion	29%	31%	33%	36%	38%	40%	43%
Annular fissure	19%	20%	22%	23%	25%	27%	29%
Facet degeneration	4%	9%	18%	32%	50%	69%	83%
Spondylolisthesis	3%	5%	8%	14%	23%	35%	50%

AJNR Am J Neuroradiol. 2015 April; 36(4): 811–816. doi:10.3174/ajnr.A4173.

Disc protrusion



The Longitudinal Assessment of Imaging and Disability of the Back (LAIDBack) Study

Jeffrey J. Jarvik, MD, MPH,*†‖ William Hollingworth, PhD,# Patrick Heagerty, PhD,‖ David R. Haynor, MD, PhD*‖ and Richard A. Deyo, MD, MPH†‖

SPINE Volume 26, Number 10, pp 1158–1166
©2001, Lippincott Williams & Wilkins, Inc.

Prevalence of degenerative findings on Lumbar MRI:

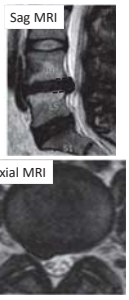
- 148 volunteers
- All asymptomatic at time of MRI
- 46% reported never having back pain

Age under 40 years:
- 5 in 10 have disk degeneration
- 3 in 10 have disk signal loss (desiccation)
- 3 in 10 have disk height loss
- 4 in 10 have a bulging disk
- 3 in 10 have a disk protrusion

Age under 40-60 years:
- 8 in 10 have disk degeneration
- 7 in 10 have disk signal loss (desiccation)
- 6 in 10 have disk height loss
- 6 in 10 have a bulging disk
- 3 in 10 have an annular fissure
- 3 in 10 have a disk protrusion

Age over 60 years:
- 9 in 10 have disk degeneration
- 9 in 10 have disk signal loss (desiccation)
- 8 in 10 have disk height loss
- 8 in 10 have a bulging disk
- 4 in 10 have an annular fissure
- 4 in 10 have a disk protrusion
- 4 in 10 have facet degeneration
- 3 in 10 have spondylolisthesis

Disc herniation: Protrusion

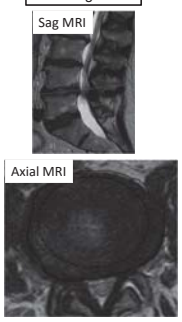


A disc protrusion (red) involves less than 25% of the disc circumference and has a wide base of attachment.

Disc herniation: Extrusion

To qualify as a disc extrusion (red) the neck of the disc material must be narrower than the material outside the disc space .

Diffuse disc bulge



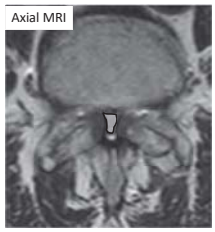
A diffusely bulging disc (red) involves greater than 25% of the disc circumference.

Disc herniation: Schmorl node

An intravertebral disc herniation (red) aka Schmorl node.

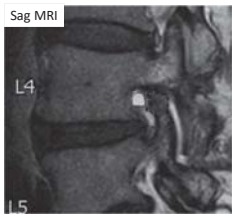
Facet joint degeneration

Facet joint hypertrophy



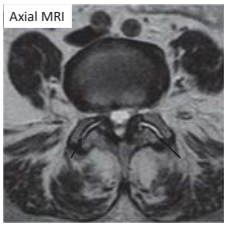
Facet joints enlarge with degeneration (red). There is central canal stenosis (blue) from the hypertrophy.

Facet joint osteophyte



This spur/osteophyte of the facet (red) extends into the neural foramen and encroaches on the nerve root (pink).

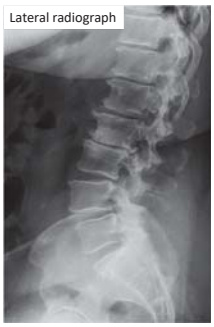
Facet joint effusion



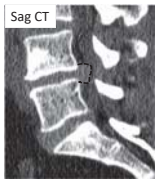
Fluid is bright on T2-weighted MRI (yellow). Fluid is not normally visible in the facet joint space, though can be seen in joint degeneration.

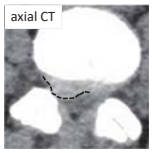
Spine Imaging and Aging: Radiography, CT, MRI

Multilevel degenerative changes

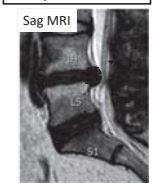


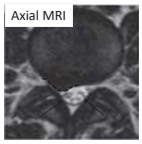
Disc protrusion, CT





Disc protrusion, MRI





Spine Imaging and Aging: Question

35-year-old otherwise healthy male presents with 1 week history of acute onset LBP radiating to left leg along the left L5 distribution that started while lifting a heavy box. Which is the most appropriate imaging study?

A. No imaging is indicated
B. Lumbar spine radiographs
C. Lumbar spine CT
D. Lumbar spine MRI

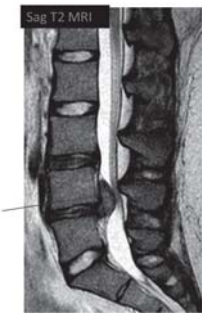
Spine Imaging and Aging: Question

You advise him that the natural history of acute LBP is to resolve in a few weeks time with conservative therapy and no imaging is need. He pays out of pocket for spine MRI and it shows a disc extrusion, likely accounting for his radicular pain.

What is the natural history of a disc extrusion?

A. Most enlarge over time
B. Most stay the same size over time
C. Most get smaller over time

Disc extrusion



Low Back Pain: Overview

Radiculopathy:
Symptoms due to injury of a nerve root.
Myotomal/dermatomal distribution of:
- pain
- paresthesia
- weakness

Acute low back pain (LBP) with or without radiculopathy: [1]
- Common: 80-85% lifetime incidence.
- 2nd most common cause for primary care visits (after URI).
- Leading cause of years lived with disability

ACP & APS Classissification:[2]
- Nonspecific LBP
- Back pain potentially associated with radiculopathy or spinal stenosis
- Back pain potentially associated with another specific cause

Acute: less than 6 weeks
Subacute: 6-12 weeks
Chronic: greater than 12 weeks

1. Murray CJ, Lopez AD. Measuring the global burden of disease. *N Engl J Med.* 2013;369(5):448-457.
2. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. Ann Intern Med. 2007;147(7):478-491.

Low Back Pain: When to image.

Uncomplicated acute LBP +/- radiculopathy:
- benign, self-limited condition
- imaging studies not warranted [1,2,3].

When to consider imaging LBP:
- After 6 weeks of medical management and physical therapy with little/no improvement & intervention candidate.
- patients with red flags of a serious underlying condition:
  - Cauda equina syndrome (saddle anesthesia, urinary retention, bowel dysfunction, bilat leg weakness)
  - Malignancy (personal hx of cancer, unexplained weight loss)
  - Fracture (trauma, tenderness to palpation, osteoporosis, prolonged corticosteroid use)
  - Infection (immunocompromised, fever, IVDU, ESR)
  - Referred pain (pancreatitis, pyelonephritis)

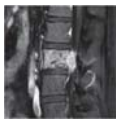
1. Chou R, Qaseem A, Owens DK, Shekelle P. Diagnostic imaging for low back pain: advice for high-value health care from the American College of Physicians. Ann Intern Med. 2011;154(3):181-189.
2. Jarvik JG, Hollingworth W, Martin B, et al. Rapid magnetic resonance imaging vs radiographs for patients with low back pain: a randomized controlled trial. Jama. 2003;289(21):2810-2818.
3. Modic MT, Obuchowski NA, Ross JS, et al. Acute low back pain and radiculopathy: MR imaging findings and their prognostic role and effect on outcome. Radiology. 2005;237(2):597-604.

"Red flag" conditions

Infection
Discitis
Osteomyelitis
Epidural abscess
Septic facet arthritis

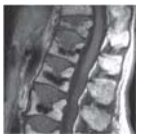
Discitis-osteomyelitis

Tumor
Metastatic to spine
Primary spine tumors
Leptomeningeal carcinomatosis
Primary cord tumors



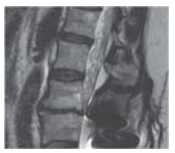
Metastatic disease

Trauma
Compression fracture



Compression fractures

Cauda Equina Syndrome



Cauda equina compression

MRI spine without and with IV contrast is indicated for evaluation of suspected:
- Tumor
- Infection

CT/MRI spine without IV contrast is indicated for evaluation of suspected:
- Degenerative disease
- Trauma

Imaging Low Back Pain: Consensus Recs

Society	*Choosing Wisely* Recommendation Regarding the Use of Imaging for Patients With Low Back Pain
American Academy of Physical Medicine and Rehabilitation	Don't order an imaging study for back pain without performing a thorough physical examination.
American Association of Neurological Surgeons and Congress of Neurological Surgeons	Don't obtain imaging (plain radiographs, magnetic resonance imaging, computed tomography [CT], or other advanced imaging) of the spine in patients with non-specific acute low back pain and without red flags.
American College of Occupational and Environmental Medicine	Don't initially obtain X-rays for injured workers with acute non-specific low back pain.
American Society of Anesthesiologists—Pain Medicine	Avoid imaging studies (MRI, CT, or X-rays) for acute low back pain without specific indications.
American Academy of Family Physicians	Don't do imaging for low back pain within the first six weeks, unless red flags are present.
American College of Physicians	Don't obtain imaging studies in patients with non-specific low back pain.

Choosing Wisely: an initiative of the American Board of Internal Medicine Foundation in collaboration with more than 70 specialty society partners, promotes a "national dialogue on avoiding wasteful or unnecessary medical tests, treatments and procedures" by publishing recommendations from the specialty societies to "facilitate wise decisions about the most appropriate care based on a patient's individual situation."

Accessed from https://www.ncqa.org

Imaging Low Back Pain: ACR Recs

American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: Low Back Pain

Variant 1: Acute, subacute, or chronic uncomplicated low back pain or radiculopathy. No red flags. No prior management.

Radiologic Procedure	Rating	Comments	RRL*
MRI lumbar spine without contrast	2		O
X-ray lumbar spine	2		☢☢☢
X-ray myelography and post myelography CT lumbar spine	2		☢☢☢☢
Tc-99m bone scan with SPECT spine	2	If there is concern for spondylolysis in a young patient, SPECT/CT remains the gold standard.	☢☢☢
CT lumbar spine without contrast	2		☢☢☢
CT lumbar spine with contrast	2		☢☢☢
MRI lumbar spine without and with contrast	2		O
CT lumbar spine without and with contrast	1		☢☢☢☢

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate — *Relative Radiation Level

https://acsearch.acr.org/list

ACR Appropriateness criteria

Clinical Condition: Low Back Pain

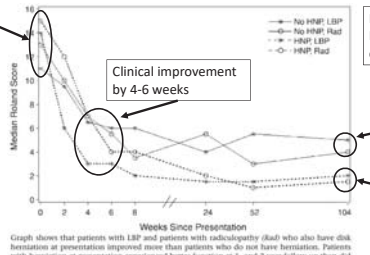
Variant 4: Acute, subacute, or chronic low back pain or radiculopathy. Surgery or intervention candidate with persistent or progressive symptoms during or following 6 weeks of conservative management.

Radiologic Procedure	Rating	Comments	RRL*
MRI lumbar spine without contrast	8		O
CT lumbar spine with contrast	5	MRI is preferred. CT is useful if MRI is contraindicated or unavailable and/or for problem solving.	☢☢☢
CT lumbar spine without contrast	5	MRI is preferred. CT is useful if MRI is contraindicated or unavailable and/or for problem solving.	☢☢☢
MRI lumbar spine without and with contrast	5	This procedure is indicated if noncontrast MRI is nondiagnostic or indeterminate. Contrast is indicated if patient has history of prior lumbar surgery. See variant 5.	O
X-ray myelography and post myelography CT lumbar spine	5	MRI is preferred. This procedure can be indicated if MRI is contraindicated or nondiagnostic.	☢☢☢☢
X-ray lumbar spine	4	This procedure is usually not sufficient for decision making without MR and/or CT imaging but can be helpful in surgical planning.	☢☢☢
Tc-99m bone scan with SPECT spine	4	This procedure can be particularly useful for facet arthropathy or stress fracture. SPECT/CT can be useful for anatomic localization and problem solving.	☢☢☢

Low Back Pain Imaging: The evidence behind the guidelines.

246 patients
- acute LBP
- +/- radiculopathy

Roland Morris Disability Questionnaire:
- Patient questionnaire
- health status measure for LBP



Graph shows that patients with LBP and patients with radiculopathy (Rad) who also have disk herniation at presentation improved more than patients who do not have herniation. Patients with herniation at presentation experienced better function at 1- and 2-year follow-up than did patients without herniation. *HNP* = herniation of nucleus pulposus.

Clinical improvement by 4-6 weeks

Re: therapeutic decision making: MRI did not have additive value over clinical assessment.

Those without disc herniation on MRI fared slightly worse.

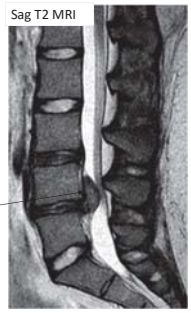
Those with disc herniation on MRI improved more.

Modic MT, Obuchowski NS, Ross JS et al. Acute low back pain and radiculopathy: MR imaging findings and their prognostic role and effect on outcome. Radiology 2005;237 (2):597-604.

Low Back Pain: Guidelines.

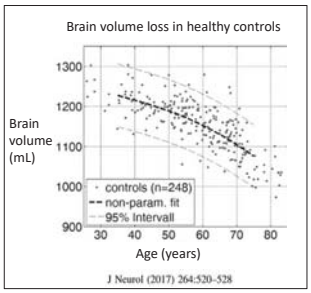
Most pt with radicular symptoms recover in several weeks[1,2].

Natural history of disc herniations is spontaneous resorption[1].
- 1/3rd regress or disappear at 6 weeks
- 2/3rd regress or disappear at 6 months

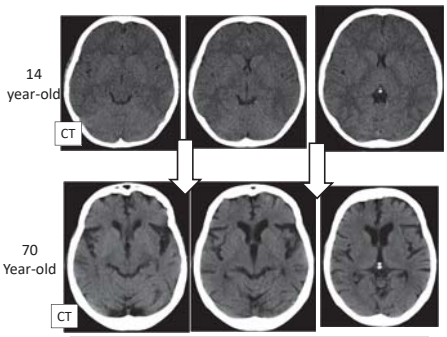


1. Modic MT, Obuchowski NS, Ross JS et al. Acute low back pain and radiculopathy: MR imaging findings and their prognostic role and effect on outcome. Radiology 2005;237 (2):597-604.
2. Pengal LH, Herbert RD, Maher CG, Refshange KM,. Acute Low Back Pain. A Systematic Review of its Prognosis. BMJ 2003:326 (7401):323

Changes with Age: Physiologic brain volume loss

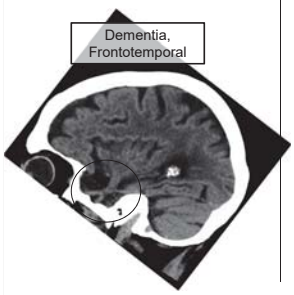


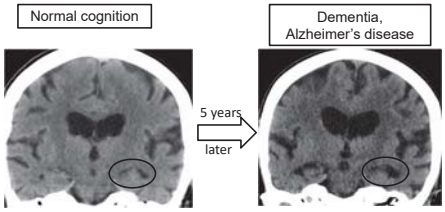
Annual brain volume loss:
Normal aging 0.5%



Physiologic, age-related, parenchymal volume loss

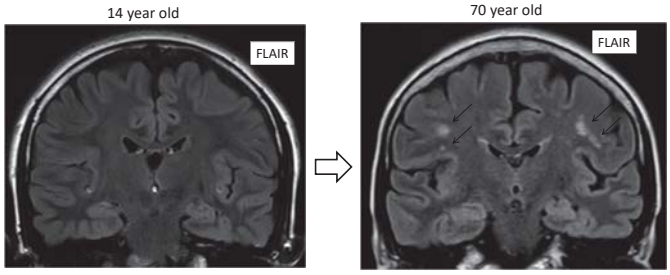
Changes with Age: Pathologic brain volume loss





Annual brain volume loss:
Normal aging 0.5%
Mild cognitive impairment 1-2%
Alzheimer's disease 2-4%

Changes with Age: Chronic small vessel ischemic changes



Normal MRI

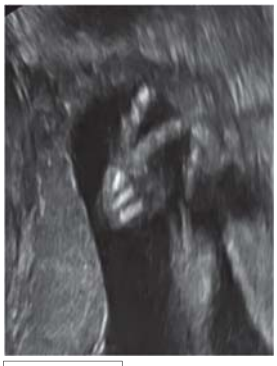
FLAIR hyperintense lesions (red) appear with age. A few spots are "allowed" in normal aging. Too many spots can be pathologic, associated with vascular dementia.

Learning Objectives: Summary

<u>Degenerative changes on spine imaging</u>
- Common & increase with age
- Not predictive of disease/symptoms
- MRI very sensitive
- Significance depends on clinical data (low specificity)
- Symptomatic disc herniations usually regress

<u>Low back pain</u>
- Common
- When to get MRI?
  - Red flag conditions (tumor, infection, fracture, cauda equina syndrome
  - Pain same/worsened > 6 weeks & surgical candidate

<u>Age-related changes on brain imaging</u>
- Volume loss is normal
- A few white matter spots are normal



Ultrasound - fetus

Peace out.

Navigating Buprenorphine in Primary Care and Encouraging your ED to Start Saving Lives!*

*with thanks to Dr. Jessica Gregg, Dr. Jonathan Robbins and Dr. Brian Garvey

DATE: Feb 15, 2020
PRESENTED BY:
Allison Fox, FNP, APRN, Senior Clinical Instructor
Laurel Hallock Koppelman, DNP, FNP, APRN, Assistant Professor

Introductions

- Allison Fox, Senior Clinical Instructor, OHSU Family Medicine at Richmond
- Laurel Hallock Koppelman, Assistant Professor, OHSU Family Medicine at Richmond
- WAIVED BUPRENORPHINE Rx'ers since 2017
- OHSU Carpool Karaoke Winners 2019

Introductions

- How many are NPs? PAs? MDs?
- Rural vs Urban?
- Waived? Already rx'ing?
- Still on the fence?
  - What would push you to prescribe?
  - Why did we decide to become prescribers?

Objectives

- Describe the current opioid crisis.
- Understand the importance of incorporating opioid use disorder treatment into primary care practice.
- Cover requirements for prescribing buprenorphine in primary care, ramifications as well as pitfalls.
- Develop prescribers who are passionate about social justice and equity for all Oregonians.

Objectives

- **The What:** What's the problem?
- **The Why:** Why it happened and why you should help.
- **The How:** How you can help.

The what: Public Health Crisis Nationwide

- Opiate OD is now leading cause of accidental death in US.
- Death Rates are deaths per 100,000 population

The what: Public Health Crisis at Home in Oregon

- Target population: Oregon (data from NIDA 3/2019)
  - 2017: 344 overdose deaths involving opioids in Oregon
    - 8.1 deaths per 100,000 persons
    - National Rate: 14.6 deaths per 100,000 persons.
  - 2015-2017:
    - Heroin deaths ⬆
    - Fentanyl deaths ⬆
    - Prescription opioid-involved overdose deaths ⬇
  - YET STILL, OREGON WROTE
    - 66.1 opioid prescriptions for every 100 persons in 2017
    - average U.S. rate of 58.7 prescriptions*
  - *This is the lowest rate in the state since 2006 when data became available (CDC).
- https://www.drugabuse.gov/opioid-summaries-by-state/oregon-opioid-summary

The what: Public Health Crisis in the Metro

- In 2018, >3 people/wk (183) died from an opioid OD in the Tri-County region (Clackamas, Multnomah, Washington)
- Most deaths
  - 72% occurred in Multnomah County
- OD death rates were higher for males compared with females, and highest for those aged 45-54

Could this be "The Why?"

9

Could this be "The Why?"

Source:
https://www.medscape.org/viewarticle/465833

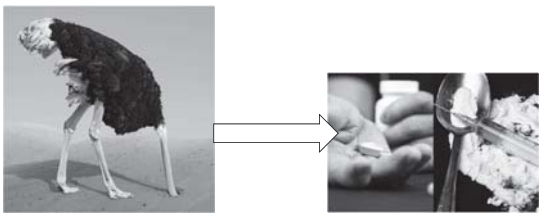
10

Could this be "The Why?"

- Reminder that people with higher ACE scores (Adverse Childhood Experiences) >=4 have a 10x greater risk factor for SUD.
- Abuse (Emotional, Physical, Sexual); Neglect (Emotional, Physical)
- Household Challenges (Mother treated violently, household substance use, mental illness in household, parents separate or divorce, criminal household member)

11

Could this be "The Why?"



12

The How: Disease Treatment

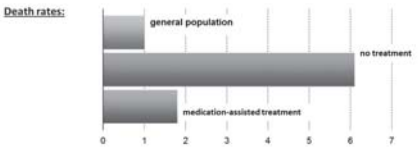
- Treat Substance Use Disorder (SUD) like a chronic illness
  - Provide preventive and comprehensive care in Emergency Rooms and **especially** in **primary care**
  - Behavioral/Mental health access
  - Medications for treatment

The How: Medications

- Methadone, Buprenorphine, and Naltrexone
  - known as medication assisted treatment (MAT)*
- Other names to use:
  - Medication for Opioid Use Disorder (MOUD)
  - Buprenorphine treatment
  - Medication
- * we will use MAT nomenclature in our presentation only b/c this is what SAMHSA still uses and will correspond to future waiver training. We don't agree with the name.

The How: Decreased Mortality with Meds

- Death rates of the general population to those who did not receive treatment for OUD
  - 1: 6
- Death Rates amongst those who received MAT for OUD and those that didn't.
  - 1.5: 6



Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017

The How: Medication Waivers

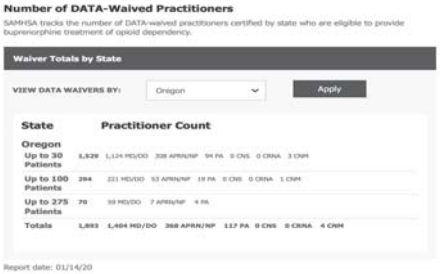
- Drug Enforcement Administration (DEA)
  - Need a DEA number
  - After training you get an X waiver
  - An X waiver allows you to prescribe buprenorphine for Opiate Use Disorder (OUD)

*you can start the training without a DEA number; get your students to start training!

The How: Medication Waivers

- DATA 2000 – Drug Addiction Treatment Act
  - Physicians can prescribe buprenorphine for OUD with 8 hours of training
- CARA 2016- Comprehensive Addiction & Recovery Act
  - NPs and PAs can rx buprenorphine for OUD with 24 hours of training starting 2017 temporarily
- CARA 2.0 in 2018
  - NPs and PAs can rx bupe permanently. CNS, CRNA and CNMs can rx bupe. Still need 24 hours.

The How: Oregon Steps Up



https://www.samhsa.gov/medication-assisted-treatment/practitioner-program-data/certified-practitioners

How to get your X-waiver

-Free Training

ASAM
https://www.asam.org/education/live-online-cme/waiver-qualifying-training

AAAP
https://www.aaap.org/clinicians/education-training/mat-waiver-training/

APNA
https://www.apna.org/m/pages.cfm?pageid=6197

AANP
https://aanp.inreachce.com/SearchResults?searchType=1&category=e5f98b0f-eafe-4f64-9779-383732cd8a10

Free as part of this conference and through PCSS
https://pcssnow.org/medication-assisted-treatment/

Diagnosing:

Substance Use Disorder (SUD) and Opioid Use Disorder (OUD)

DSM 5: How to diagnose SUD and OUD

- DSM
  - 11 criteria
    - 4 categories
      - Craving
      - Compulsion
      - Consequences
      - Loss of control

DSM 5: How to diagnose SUD and OUD

- DSM
  - 11 criteria
    - 4 categories
      - Craving/Compulsion
        1. Taking in larger amounts or for longer than intended
        2. Unsuccessful efforts to cut down
        3. Spending a lot of time obtaining the substance
        4. Craving or a strong desire to use the substance
      - Consequences
      - Loss of control

DSM 5: How to diagnose SUD and OUD

- DSM
  - 11 criteria
    - 4 categories (the 4 C's)
      - Craving
      - Compulsion
      - Consequences/Loss of control
        5. Continued use despite recurring social or interpersonal problems due to use
        6. Important activities given up or reduced
        7. Recurrent use in physically hazardous situations
        8. Persistent/Recurrent physical or psychological difficulties from use
        9. Recurrent use resulting in a failure to fulfill major role obligations

DSM 5: How to diagnose SUD and OUD

- DSM
  - 11 criteria
    - 4 categories
      - Craving
      - Compulsion
      - Consequences
      - Loss of control

        10. Tolerance*
        11. Withdrawal*

DSM 5: How to diagnose SUD and OUD

- DSM
  - 11 criteria
    - 2-3 criteria: MILD DISORDER
    - 4-5 criteria: MODERATE DISORDER
    - 6+ criteria: SEVERE DISORDER

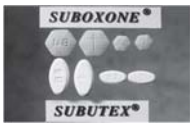
Understanding: Buprenorphine for Opioid Use Disorder (OUD)

Buprenorphine: How does it work?

Buprenorphine has unique pharmacological properties that help:
- Lower potential misuse
- Diminish the effects of physical dependency to opioids, such as withdrawal symptoms and cravings
- Increase safety in cases of overdose

Buprenorphine is not a substitute for methadone, it is one more choice on the treatment menu

Both should be used in a comprehensive treatment setting



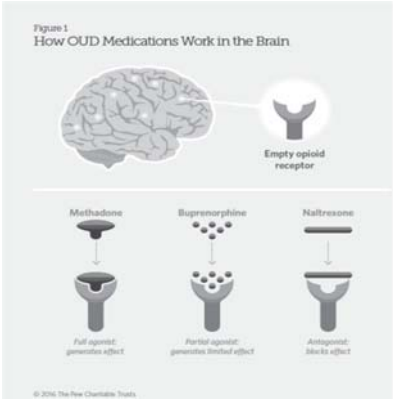
Pharmacology

Buprenorphine has a strong affinity (affinity = strength of a drug to physically bind to receptor) to the opioid mu receptor. Meaning: it will displace other opioids from the mu receptor resulting in acute opioid withdrawal

Naloxone is added to buprenorphine (Combo = Suboxone) to decrease likelihood of diversion. It is taken as SL tabs, not swallowed due to poor GI bioavailability; naloxone SL has no effect

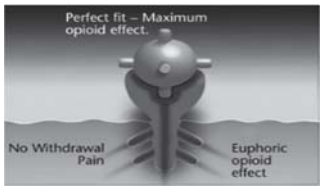
"Ceiling effect"
- Lowers risk of misuse, dependency and side effects

Long-acting
- Mean half-life 37 hours, range 20-70 hours



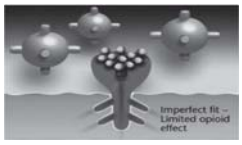
- Opioid receptor is empty: whenever there is insufficient amount of opioid receptors activated, the person will feel pain. This happens when someone is going through withdrawal
- Once dependent the body cannot produce enough natural opioids to satisfy the new receptors formed from large doses of opiates over time

Courtesy of NAABT, nc. (naabt.org) The National Alliance of Advocates for Buprenorphine Treatment



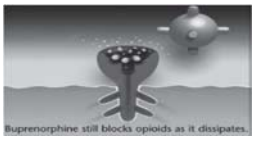
- Opioid receptor is filled with a full-agonist.
- The strong opioid effect of heroin and opiates can cause euphoria and will stop withdrawal for 4-24 hours.

Courtesy of NAABT, nc. (naabt.org)



- Opioids replaced and blocked by buprenorphine.
- Buprenorphine competes with the full agonist opioids for the receptor. Since it has a higher affinity (stronger binding ability) it expels existing opioids and blocks others from attaching
- As a partial agonist, the buprenorphine has a limited opioid effect, enough to stop withdrawal but not enough to cause intense euphoria

Courtesy of NAABT, nc. (naabt.org)



- Over time (24-72 hours) buprenorphine dissipates, but still creates a limited opioid effect (enough to prevent withdrawal) and continues to block other opioids from attaching to the opioid receptors. If someone takes opioids they wouldn't get high
- At a certain point, the increasing effects of partial agonists reach maximum levels and do not increase further, even if doses continue to rise- the ceiling effect
- As higher doses are reached, partial agonists can act like antagonists- occupying receptors but not activating them (or partially activating them) but still blocking full agonists

Courtesy of NAABT, nc. (naabt.org)

Buprenorphine RECAP

- Partial Agonist at MU receptor
  - Minimal respiratory suppression
- Long Acting
  - Half life 24-36 hours
- High Affinity for MU receptor
  - Blocks
  - Displaces
- Slow dissociation
  - Stays for a long time

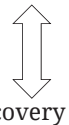
Buprenorphine Forms

- Buccal and Sublingual Films
- Tablets (NOT TO SWALLOW)
- Implants*
- Sub Q Injection*
- Formulations are:
- MONO PRODUCT
  - For pregnant women (sometimes)
  - WITH NALOXONE-first line
    - To help with diversion.
    - If crushed and injected, person will go into withdrawal.
    - There is NO BIOAVAILABILITY of naloxone if used orally
      - IN other words, a person will not go into withdrawal using SUBOXONE from the naloxone in the product if they use it appropriately.

*insurance dependent
***transdermal patch not for OUD

How to decide how and who you treat?

- Harm reduction



- Recovery with abstinence from all substances.

Buprenorphine Treatment

Who's a candidate?

- Have been objectively diagnosed with an opioid use disorder
- Are willing to follow safety precautions for the treatment
- Have been cleared of any health conflicts with using buprenorphine
- Have reviewed other treatment options before agreeing to buprenorphine treatment

Buprenorphine Treatment

- Costs and reimbursement
  - Behavioral Health staff-not required!
  - Point of Care Urine Drug Screening-not required!
  - Monitoring labs
- False positives and negatives, need for confirmation labs
- DIVERSION – consider random call ins!
- Lack of engagement – do we only want people who want the help?
- Is your staff ready/willing/able–training? Trauma Informed Care?

Stigmatizing language

- Instead of
  - MAT……..say MEDICATION
  - Addict/Junkie/Drug Abuser….say person with OUD or SUD
  - Clean or Dirty Urine……..say Urine as expected or Urine with buprenorphine and benzos
  - Relapsed…..say had a setback or **SLIP**
  - Ex-Addict……say in recovery
  - Medication is a crutch…..say medication is a treatment tool.

Stigmatizing language.

https://www.recoveryanswers.org/research-post/the-real-stigma-of-substance-use-disorders/

Indications for Declining Treatment

- ~~Benzodiazepine dependence~~
- ~~Alcohol dependence~~

  - As of 9/2017 FDA changes recommendations
  - Bupe and methadone should not be withheld b/c patients taking benzos or drugs that depress CNS
  - Always DOCUMENT that you discussed increase risk of serious side effects and even death.
  - Harm caused by untreated OUD outweighs risks

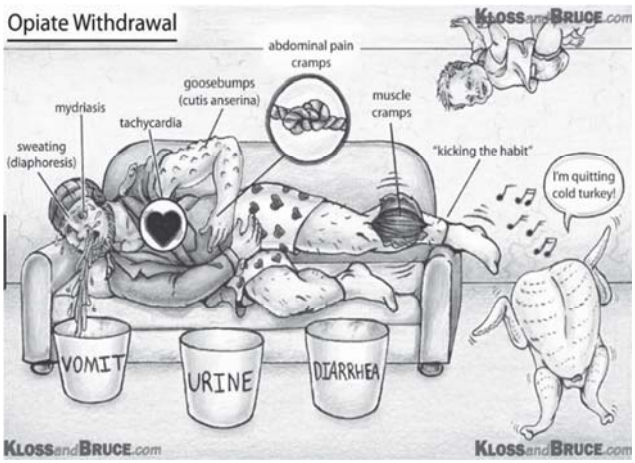
- Failure to commit to frequent check ins
- Coming to program for pain or because they want more opiates
  - Concern for using buprenorphine to fund other habits (meth)
- Refuse to acknowledge OUD/SUD
- Doesn't MEET DSM 5 criteria

Treating with Buprenorphine- 3 phases

- **Phase 1: Induction-** in office or at home (if not bupe naïve)
- **Phase 2: Stabilization-** cravings are gone, patient is experiencing few if any side effects. Dose may need to be changed, delivery (tabs, film, subutex)
- **Phase 3: Maintenance-**when someone is doing well on a steady dose of buprenorphine. You can decide a time frame for bupe treatment, although some people do need lifetime. Time to engage in treatment for rehabilitation to prevent setbacks***

Treating with Buprenorphine- INDUCTION

- **Goal: Find dose of buprenorphine that reduces cravings and withdrawal symptoms, minimal side effects if any and helps to reduce use of other opioids.**



Treating with Buprenorphine- INDUCTION in the office

- Tell the patient to come to the office already in withdrawal
- This ensures that they won't have a PRECIPITATED withdrawal if you give them buprenorphine
  - 12-16 hours free of short acting opioids
  - 24 hours for heroin or long acting opioids
  - 36 hours for methadone
- **Document withdrawal using Clinical Opiate Withdrawal Scale (COWS)**

Treating with Buprenorphine- INDUCTION in the office COWS

- Resting Pulse
- Sweating
- Restlessness
- GI Upset
- Tremor
- Pupil Size
- Bone or Joint aches
- Yawning
- Anxiety or Irritability
- Gooseflesh
- Runny Nose
- Tearing Eyes


Clinical Opiate Withdrawal Scale (COWS)

Flow-sheet for measuring symptoms over a period of time during buprenorphine induction.

For each item, write in the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name: _____ Date: _____

Buprenorphine induction:

Enter scores at time zero, 30min after first dose, 2 h after first dose, etc.

Time: _____ _____ _____ _____

Resting Pulse Rate: (record beats per minute) Measured after patient is sitting or lying for one minute 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120				
Sweating: over past ½ hour not accounted for by room temperature or patient activity. 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face				
Restlessness Observation during assessment 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds				
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible				
Bone or Joint aches If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/ muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort				
Runny nose or tearing Not accounted for by cold symptoms or allergies 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks				

Treating with Buprenorphine- INDUCTION in the office STEP 1

- COWS of at least 8; the higher the better!
  - Not in withdrawal? Wait……send home until next day or….. home induction.
- BEWARE fentanyl. COWS 13-15 is better goal.
- Administer 2-4 mg bupe (under the tongue if a tab; in buccal mucosa if strip/film)
- no food or drink other than water
- Wait until fully dissolved then can swallow or spit out residual
- should feel relief in 40 minutes.

Treating with Buprenorphine- INDUCTION in the office STEP 1

- If patient goes into precipitated withdrawal
  - STOP the induction, meds for symptoms to home and return next day

OR

- Give ANOTHER dose of buprenorphine (PREFERRED)

Treating with Buprenorphine- INDUCTION in the office STEP 2

- Monitor patient for 2 hours after first dose
- Give 2-4 additional mg of bupe every 2-4 hours if withdrawal returns.
- Typical dosing is 8-16mg on first day.
- Day 2: use Day 1 dose plus 4 mg (if needed)
  - Have RN call pt to evaluate
- Day 3: use Day 2 dose plus 4 mg (if needed)
  - Schedule an office visit or provider phone call to check in.
- Day 8: schedule follow up to evaluate for side effects/cravings.

- Typical daily dose: 8-16mg
- Maximum dose: 24 mg.

Treating with Buprenorphine- INDUCTION in the office METHADONE

- Confirm 36 hours from last dose of methadone (must be on 30mg or less of total methadone daily)
- Give 2mg dose to start.
- SLOW induction to reduce chance of precipitated withdrawal.

Treating with Buprenorphine- INDUCTION (repeated)

- **Goal: Find dose of buprenorphine that reduces cravings and withdrawal symptoms, minimal side effects if any and helps to reduce use of other opioids.**

- **Typical doses range from 8mg to 16mg***
  ***10% of people need 24mg (heroin use)**

Treating with Buprenorphine- Meds for withdrawal symptoms

- **Clonidine for Anxiety/Restlessness**
- **Trazodone for Insomnia**
- **Acetaminophen/Ibuprofen for MSK pain (sometimes tizanidine)**
- **Ondansetron, loperamide, push fluids for N/V/Diarrhea**

Treating with Buprenorphine- Don't Forget Naloxone

Richmond MAT Program

Richmond MAT Program

- 1 Federally Qualified Health Center
- 375 patients in program
- 18 prescribers (NPs, PAs, MDs)
- 1 dedicated RN
- 2 Behavioral Health Consultants
- 1 panel coordinator

OHSU

Family Medicine at Richmond

Richmond MAT Program

- Tier system: refills and PCP/MAT team member visits
  - Tier1: weekly
  - Tier 2: 2 weeks
  - Tier 3: monthly
  - Tier 4: bi-monthly
  - Tier 5: visits every 3 months
  - Tier X: discharged from program
  - Tier Y: lost from program

Richmond Rapid Response Program

- Create a Fast-Track entry partnership between OHSU ED and Family medicine at Richmond's MAT
- Patients may establish care with a PCP (NP/PA/MD) within 24-72 hours of induction in the ED.
- Buprenorphine prescription continues.

Richmond Rapid Response Program

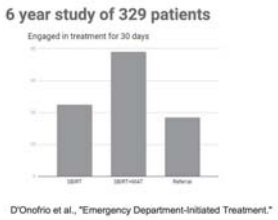
- Initiation of buprenorphine in the Emergency Department (ED) prevents recidivism/lengthens engagement.
- Primary care is the appropriate place to treat opioid use disorder (OUD).
  - Access to mental health, legal, housing resources and treat co-morbidities/screening
- System Level factors to prevent transitions of care and access to ongoing treatment.

Richmond Rapid Response: Fast track protocol

- Pt is identified as appropriate for bupe induction in ED
- Rx for up to 7 days provided by ED provider
- SW/RN/Provider calls Emma Abiles at OHSU Richmond: 503-418-3900
- Appt made for 24-72 hour f/up with new PCP
- **After Hours:
  - Confirm pt's contact info.
  - Chart is routed to FM RICHMOND MAT
  - Emma will call pt. to schedule visit w/in 24-72 hour time frame of d/c.

Building a Bridge to the ED

- Initiation of buprenorphine in the Emergency Department (ED) prevents recidivism/ lengthens engagement.



D'Onofrio et al., "Emergency Department-Initiated Treatment."

Building a Bridge to the ED

- Step 1:
  Conduct a needs assessment to determine:
  - –Barriers to care
  - –Infrastructure inadequacies
  - –Collaboration strategies
  - –ED interest in bupe induction

Building a Bridge to the ED

- Step 2:
  Create a channel for feedback for an expedited conduit:
  - –Collaborate with key ED personnel
  - –Develop protocol for fast track transfer
  - –Get buy in from your own clinic

Building a Bridge to the ED

- Step 3:
  - Ally buliding
    - Education about problem
    - Training for staff
    - Develop Smart Sets
    - Develop Referral program

Building a Bridge to the ED

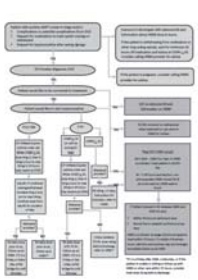
- California ED Bridge, Dr. Andrew Herring
  - https://www.bridgetotreatment.org

- Massachusetts now requires ED initiation of bupe.

Building a Bridge to the ED

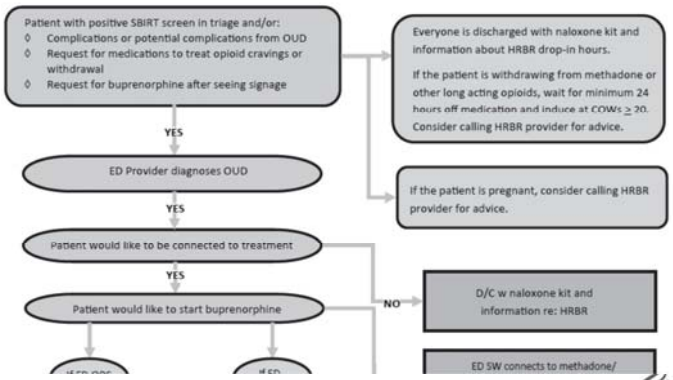
- Myth:
  - "If people know I'm prescribing buprenorphine, there will be a line out the door."
  - "I'm worried about putting someone into precipitated withdrawal."

OHSU Emergency Department-Induction Flowsheet and Order sets (please borrow)

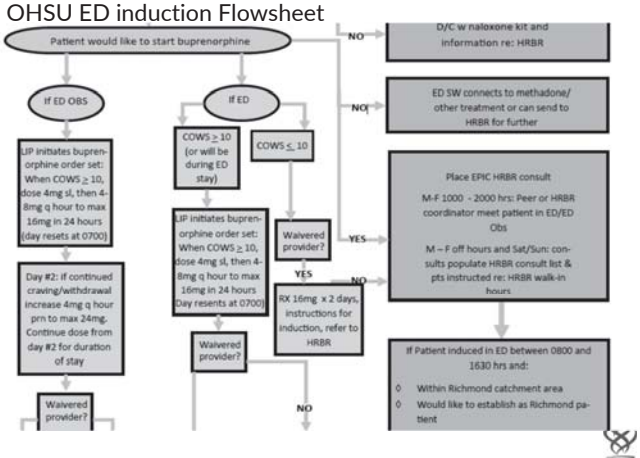


Shared with permission by Dr. Jessica Gregg, OHSU Impact Team

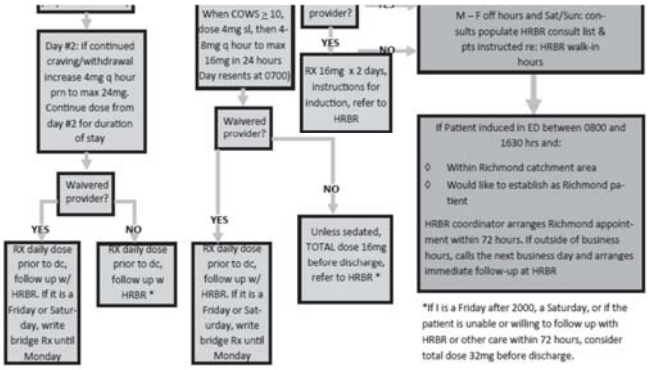
OHSU ED induction Flowsheet



OHSU ED induction Flowsheet



OHSU ED induction Flowsheet



OHSU ED Smart Set for EPIC

Coming soon: micro dosing…..

- No need to go through withdrawals or come off opioids
- Minimize risk of precipitated withdrawal

The What, The Why and The How

- Now it's up to you!

OHSU

"Evidence shows that initiation of MAT increases chance of 30 day treatment with decreases mortality."
- Alinea Stevens, MD, MPH, Care Innovations.

Questions?
Allison Fox, FNP, APRN
foxal@ohsu.edu
Laurel Hallock Koppelman, D.N.P., F.N.P.-C, APRN
hallockk@ohsu.edu

Thank You

Evidence Based Physical Therapy – An Update

Trevor Schongalla
PT, DPT, OCS

Trending

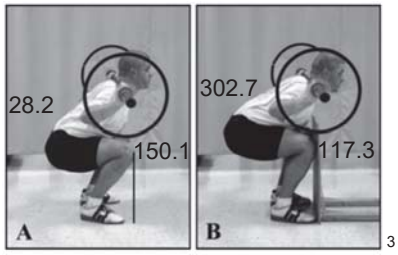
1. Patellofemoral joint pain
2. Low back pain
3. Blood flow restriction therapy
4. Ultrasound treatment

1.
Patellofemoral Joint Pain

25%

To weight-bear or not to weight-bear

973% increased hip/back torque



[3]

22% decreased knee torque

Patellofemoral Joint Pain Takeaways

- Hip strength
- Weight-bearing is allowed
- Words matter

Access Code: YDBMAW24
URL: https://OHSUrehabilitation.medbridgego.com/

2. Low back pain

33%

What's working?[2]

Manual therapy

Repeated motions

Coordination, strength, and endurance

Coordination, Strength, and Endurance

Motor control

Stabilization

Strength

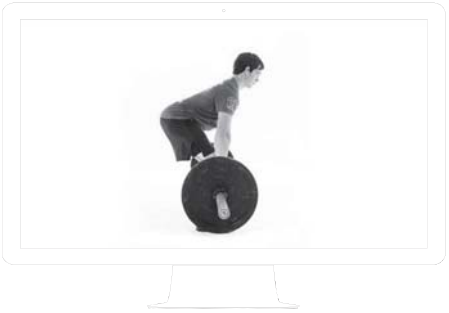
Graded exercise

Make it harder

The Classics




Deadlift?[4,5]

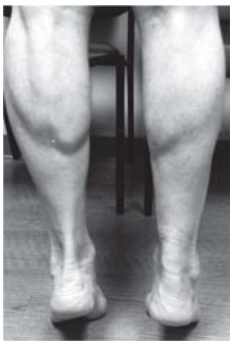


Low Back Pain Takeaways

- Education
- Valid option
- Patient specific
- Risk?

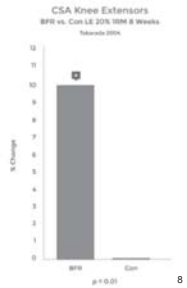
Access Code: QBZV4HG9
URL:
https://OHSUrehabilitation.medbridgego.com/

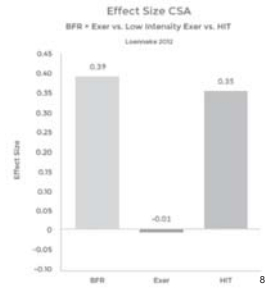

3. Blood Flow Restriction Therapy



BFR Indications

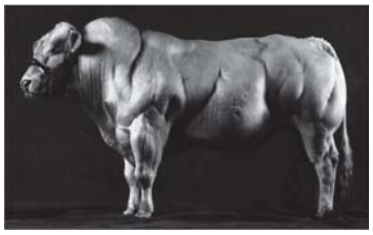

BFR Outcomes[6,7]





8 8

BFR Physiology



BFR Takeaways

- Great for strength
- Traditional strength training
- Over the counter options
- Risk?

https://www.owensrecoveryscience.com/certified-providers/

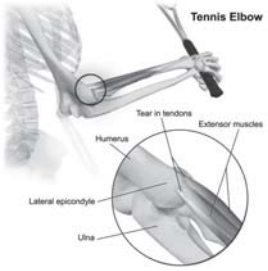
4. Ultrasound

US Metaanaylsis[11]

80%

Ultrasound has been used therapeutically for over 6 decades in the ways reported in the trials examined in this study.[73] Any clinically significant effects should, by now, have been identified in a number of rigorous studies that showed which patient outcomes are improved by using therapeutic ultrasound. In our

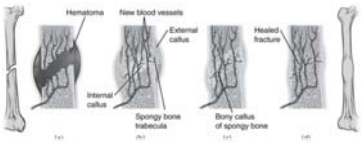
Tennis Elbow[9]



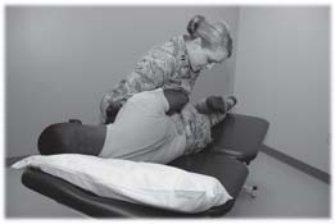
Knee OA[10]

Fracture healing[12]

64 days



Low Back Pain[13]



Ultrasound Takeaways

- Minimal to no high quality evidence
- Patient dependence

Trends

1. Patellofemoral pain
2. Low back pain
3. Blood flow restriction
4. Ultrasound

THANKS!

Any questions?

You can find me at:

- schongal@ohsu.edu

References

1. Willy RW, Hoglund LT, Barton CJ, et al. Patellofemoral Pain. J Orthop Sports Phys Ther. 2019;49(9):CPG1-CPG95.
2. Delitto A, George SZ, Van dillen L, et al. Low back pain. J Orthop Sports Phys Ther. 2012;42(4):A1-57.
3. Fry AC, Smith JC, Schilling BK. Effect of knee position on hip and knee torques during the barbell squat. J Strength Cond Res. 2003;17(4):629-33.
4. Aasa B, Berglund L, Michaelson P, Aasa U. Individualized low-load motor control exercises and education versus a high-load lifting exercise and education to improve activity, pain intensity, and physical performance in patients with low back pain: a randomized controlled trial. J Orthop Sports Phys Ther. 2015;45(2):77-85, B1-4.
5. Welch N, Moran K, Antony J, et al. The effects of a free-weight-based resistance training intervention on pain, squat biomechanics and MRI-defined lumbar fat infiltration and functional cross-sectional area in those with chronic low back. BMJ Open Sport Exerc Med. 2015;1(1):e000050.
6. Takarada Y, Tsuruta T, Ishii N. Cooperative Effects of Exercise and Occlusive Stimuli on Muscular Function in Low-Intensity Resistance Exercise with Moderate Vascular Occlusion. *The Japanese Journal of Physiology*. 2004;54(6):585-592. doi:10.2170/jjphysiol.54.585
7. Loenneke JP, Wilson JM, Marín PJ, Zourdos MC, Bemben MG. Low intensity blood flow restriction training: a meta-analysis. Eur J Appl Physiol. 2012;112(5):1849-59.
8. Owens J. Blood Flow Restriction Rehabilitation Manual.
9. Bisset L, Paungmali A, Vicenzino B, Beller E. A systematic review and meta-analysis of clinical trials on physical interventions for lateral epicondylalgia. Br J Sports Med. 2005;39(7):411-22.
10. Cakir S, Hepguler S, Ozturk C, Korkmaz M, Isleten B, Atamaz FC. Efficacy of therapeutic ultrasound for the management of knee osteoarthritis: a randomized, controlled, and double-blind study. Am J Phys Med Rehabil. 2014;93(5):405-12.
11. Robertson VJ, Baker KG. A review of therapeutic ultrasound: effectiveness studies...reprinted from Robertson VJ, Baker KG, Physical Therapy, July 2001, Vol. 81, pp. 1339-1350, with permission of the American Physical Therapy Association. Journal of Women's Health Physical Therapy. 2010;34(3):99-110. doi:10.1097/JWH.0b013e318200897a.
12. Busse JW, Bhandari M, Kulkarni AV, Tunks E. The effect of low-intensity pulsed ultrasound therapy on time to fracture healing: a meta-analysis. CMAJ. 2002;166(4):437-41
13. Seco J, Kovacs FM, Urrutia G. The efficacy, safety, effectiveness, and cost-effectiveness of ultrasound and shock wave therapies for low back pain: a systematic review. Spine J. 2011;11(10):966-77.

Iron – Too Much and Too Little

Tom DeLoughery, MD MACP FAWM
Oregon Health & Sciences University

@bloodman

GENERAL HEMATOLOGY

DISCLOSURE

Relevant Financial Relationship(s)

Speaker Bureau - None

Consultant/Research – none

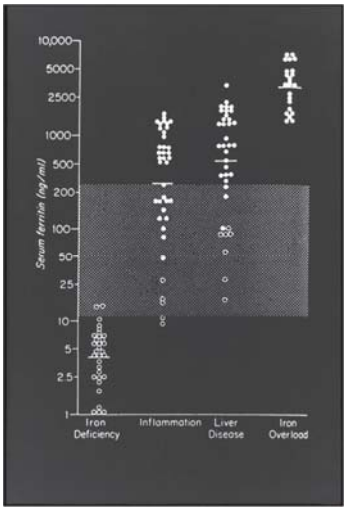
What I Will Be Talking About

- Iron Overload
- Iron Deficiency

How to Measure Iron

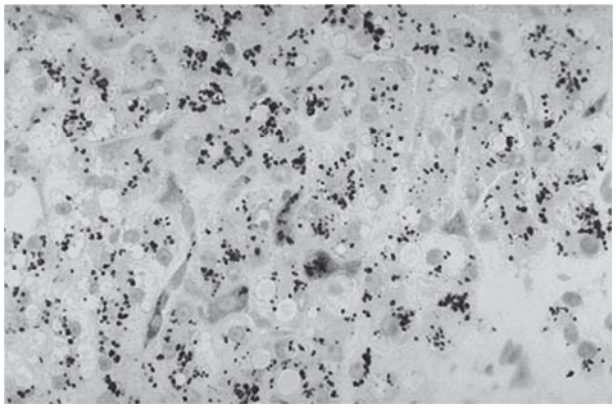
Ferritin

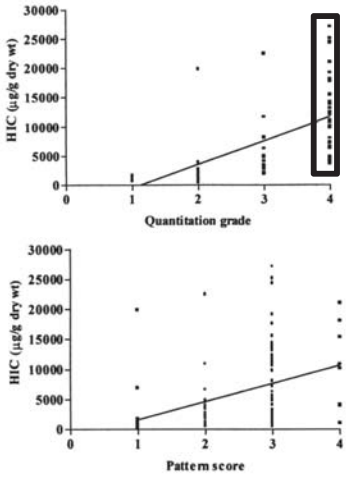
- Great for iron deficiency
- High levels worrisome for iron overload
- No relationship with high iron and amount of tissue iron



Biopsy

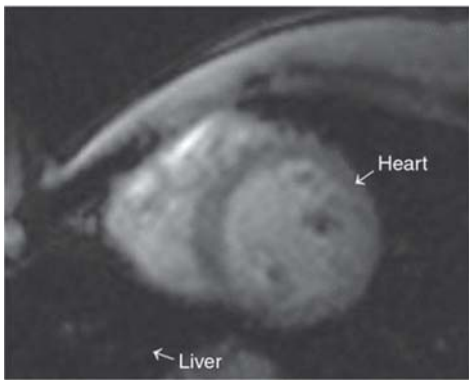
- Liver
  - Iron stain – quantitative
  - Tissue iron concentration key
- Cardiac – biopsy
- Marrow biopsy
  - Not helpful
    - Low in hemochromatosis!



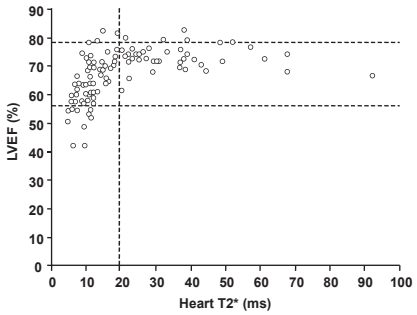


MRI

- Liver
  - Correlation with T2* scan and iron load
  - Now the go-to test
- Cardiac MRI
  - Rapidly becoming gold standard



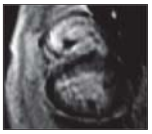
T2* MRI—New Standard for Cardiac Iron



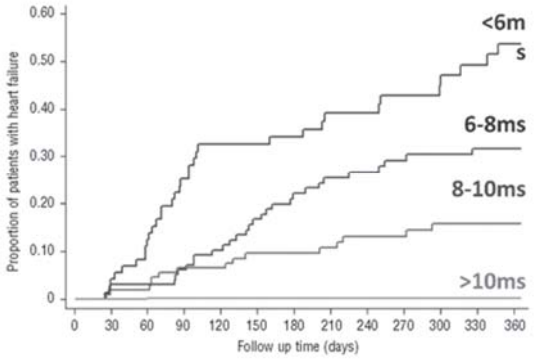
Relationship between myocardial T2* values and left ventricular ejection fraction (LVEF). Below a myocardial T2* of 20 ms, there was a progressive and significant decline in LVEF ($R = 0.61$, $P < .0001$).

Reprinted from Anderson LJ, et

Cardiac T2* value of 37 in a normal heart



Cardiac T2* value of 4 in a significantly iron overloaded heart



High Iron Labs: What to Do

- High iron saturations
- High ferritins

High Iron Saturation

- Can be influence by oral iron
- Need to repeat fasting for two hours

High Iron Saturations

- Hemolysis
  - Release of heme iron
- Iron overload
  - Genetic
  - Acquired
- Don't get too worked up if ferritin is normal

Ferritin

- Elevated levels
  - Inflammation
  - Liver disease
    - Fatty liver
  - Iron overload

Inflammation

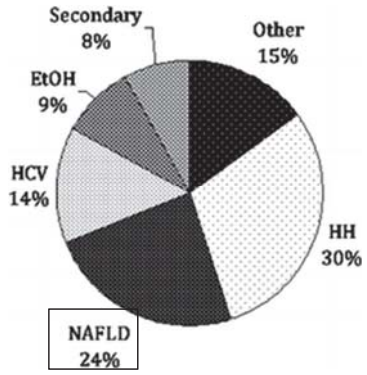
- Ferritin acute phase reactant
- Can be > 1000 ng/dl
- Testing
  - High ferritin
  - High CRP
  - Low iron saturation

Liver Disease

- Ferritin released from damage hepatocytes
- Acute liver disease
  - Very high levels
- Chronic liver disease
  - Up if liver function test up

Non Alcoholic Steatohepatitis

- Common in
  - Diabetes
  - Obesity
- High ferritins
  - Usually normal to low saturations
- Phlebotomy not helpful



Dever JB, Digestive Diseases and Sciences, Dig Dis Sci. 2010 Mar;55(3):803-7.

Alcohol

- Significant alcohol use can raise ferritin
  - Liver toxicity?
  - Increase iron absorptions
- Can be seen with > 2 drinks/day
  - > 2 beers, > 10 oz wine, > 3 oz hard stuff

Iron Overload and Hemolysis

- Occurs frequently in congenital hemolytic anemia
  - Not associated with transfusion
- Associated with increase iron absorption
- Seen in all congenital hemolytic anemias
- Seen also in alpha-thal traits

Work Up of High Ferritins

- First line
  - Saturation
    - > 50% -worrisome for iron overload
    - < 20% - inflammation
- CMP
- Alcohol history
- Hbg A1C
- Reticulocyte count

Iron Overload

- Genetic testing
- End organ damage
  - Liver bx if ferritin > 800-1000 and sats high but negative genetic tests
  - Trial of phlebotomy
  - MRI
    - Increasing use if no signs of liver disease

Genetic Hemochromatosis

- At 4 kinds of defects
- Types 1 and 4 more common
- Mutations much more common than disease

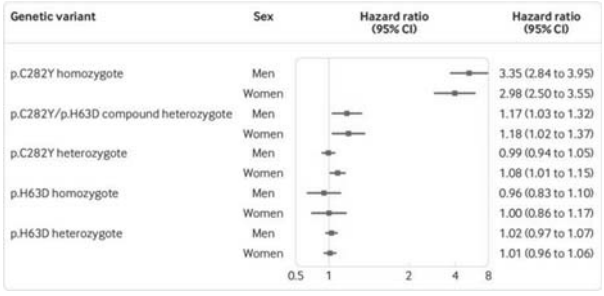
HH Type 1

- Autosomal Recessive
- Carrier frequency - 1 in 10
- Homozygotes ~ 1 in 200 Caucasians
  - 1-21% symptomatic
- Clinical manifestation
  - 5:1 males:females
  - Late onset - > 40 years
  - Defects in HFE gene
  - Liver, joints, endocrine

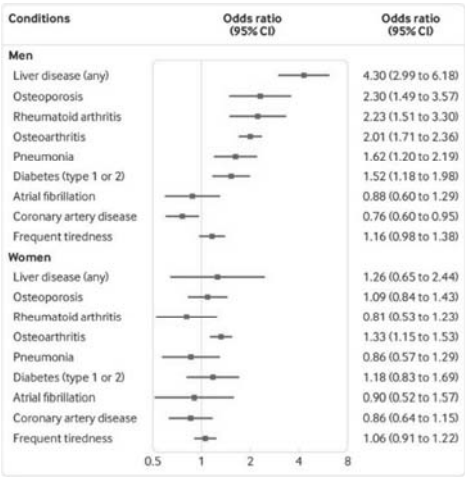
Genetics

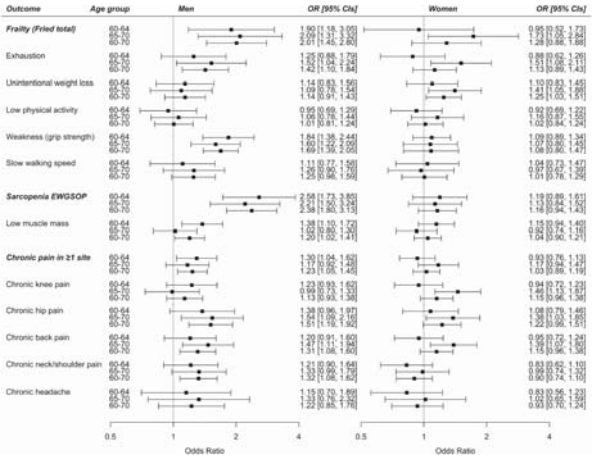
- Classic C282Y homozygous
  - Men ~ 20% penetrance
  - Women ~ 1%
- H63D/C282Y
  - ? < 1%

Forest plot of associations for developing at least one p.C282Y associated incident condition (incident haemochromatosis, liver disease (including liver cancer), diabetes (type 1 or 2), rheumatoid arthritis, or osteoarthritis) by end of follow-up, stratified by genotype and sex.



Luke C Pilling et al. BMJ 2019;364:bmj.k5222





Rarer types

- HH Type 2-4
  - 2/3 younger and severe
  - Type 4 not as severe
- Uncertain if worth screening for

Hemochromatosis NOS

- ~ 20% negative HFE
  - High ferritin
  - Tissue iron overload
- Phlebotomy

Therapy

- Inflammation
  - Primary cause
- Steatohepatitis
  - Lipid and diabetes control
  - No benefit phlebotomy
- Alcohol
  - Decrease drinking
- Iron overload
  - Phlebotomy

Therapy: Hemochromatosis

- Phlebotomy
  - Weekly in symptomatic patients
  - Weekly to biweekly in carriers if ferritin > 300
- Goals
  - Ferritins < 50
- Iron overload in congenital anemias
  - Phlebotomy if tolerated

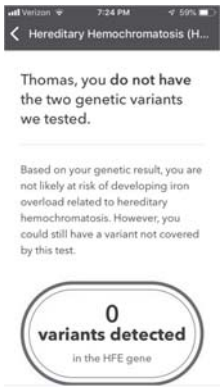
Goals of Therapy

- No end organ damage
  - Full life expectancy
- Liver cirrhosis
  - Minimal improvement
  - Screen for hepatoma

Goals of Therapy

- Cardiac
  - Reversal
- Diabetes
  - Some improvement
- Joints
  - Usually no improvement

23&Me



Work-Up

- Repeat genetics
- Ferritin
  - > 300:phlebotomy
  - < 300: yearly ferritins
  - < 50: ok to treat iron deficiency
- Family screening

Acquired Iron Overload

- Chelators
- Disease states

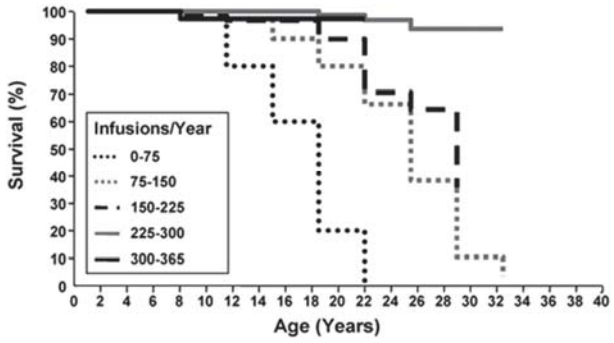
Chelating Agents

- Deferoxamine (DFO)
- Deferasirox (DX)
- Deferiprone (DP)

When to Use Chelation

Thalassemia

- Clear benefit to thal-major patients
  - Reduced cardiac toxicity
  - Reduced endocrine
- Probably benefit to thal-inter patients
- Start early!



Hematology Am Soc Hematol Educ Program. 2009:664-72.

Sickle Cell

- Very heterogenous population
- Increasing patients received multiple transfusions
  - Stroke prevention
  - Older patients with end organ damage

Sickle Cell

- Benefits of chelation very unclear
- Consider for
  - Heavily transfused younger patients
  - Sickle-thal patients
- Guided by cardiac MRI monitoring

Myelodysplasia

MDS

- Increasing recognition of lack of correlation of transfusions and iron overload
  - Reports in transfusion independent patients with RARS
  - "The rationale for iron chelation therapy in MDS remains compelling but has not been tested in prospective randomized studies." Blood 2014

MDS

- T2* MRI predictive of need for chelation and cost-effective
- Yearly on transfusion dependent patients or those with RARS

Iron Deficiency

- Common!
- Treatable

Iron

- Clear evidence of detriment of iron lack
  - Vitality
  - Exercise performance
  - Cognition
  - Restless legs
  - Hair growth

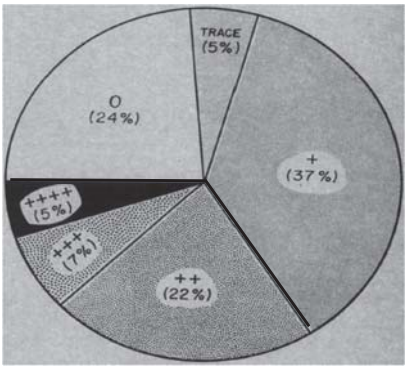
Iron for Fatigue

- Two RCT with oral iron show benefit with ferritin < 50 ng/mL
- One RCT shows benefit with either ferritin < 15 ng/mL or sats < 20%
- Should be consider for fatigue and ferritin < 50 ng/mL

Iron Requirements

- Men: 14 ug/kg/day
  - ~ 1mg/day
- Women:
  - ~2.4-3.4 mg/day
- Pregnancy
  - 3-5 mg/day

Most Women have Low Iron Stores



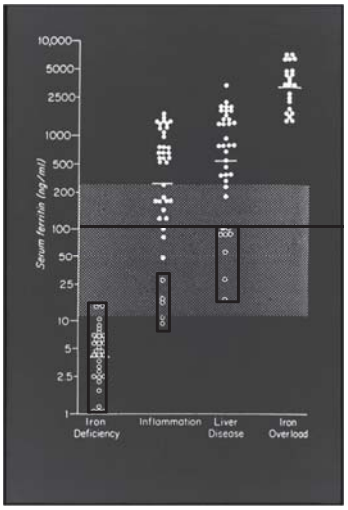
JAMA, Mar 1967; 199: 897 - 900

Iron is Good

- Iron required by every tissue
- Laboratory ranges of "normal" do not reflect physiology

Diagnosis of Iron Deficiency Anemia

- MCV
- Serum iron
- TIBC
- Iron saturation
- Ferritin
- Bone marrow tests

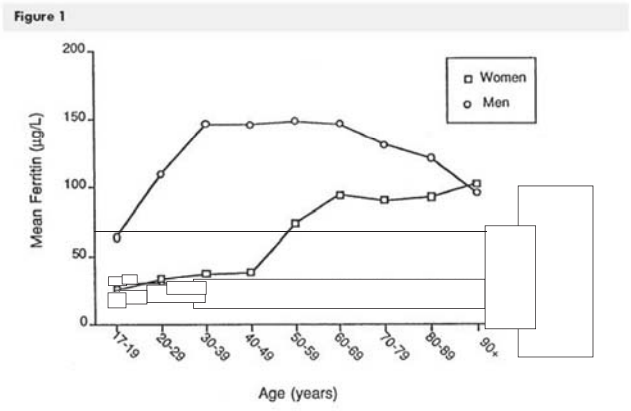


N Engl J Med. 1974 May 30;290(22):1213-6.

Iron Deficiency

- Serum ferritin is <u>BEST</u> non-invasive test of iron status
  - > 100 ng/mL rules out iron deficiency
  - Lower limit changes with age and condition
    - Patient over 65 with ferritin < 50 ng/mL <u>all</u> iron deficient

Age and Ferritin



Serum Ferritin

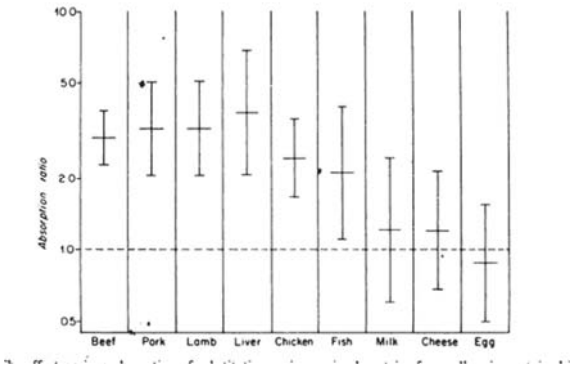
- Serum ferritin proportional to iron stores
- Needs iron to be produced
  - Acute phase reactant <u>only</u> in presence of iron
- Most accurate non-invasive test of iron stores!

Ferritin: Bottom Line

- Ignore lab reference ranges!
  - < 15 ng/ml 100% specific
  - > 100 ng/ml rules-out
- In older patients ferritins < 100ng/ml consider GI work-up
- Iron supplementation to women with ferritins < 50ng/ml improves fatigue

Dietary Iron

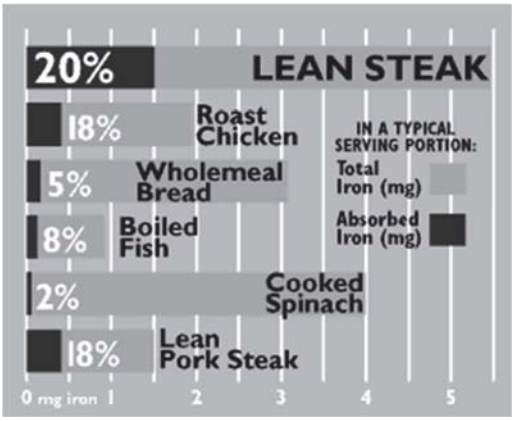
- Heme iron 10x better absorbed than non-heme iron
- Meat protein improves iron absorption



Am J Clin Nutr **August**
1976 vol. 29 no. 8
859-867

Dietary Iron

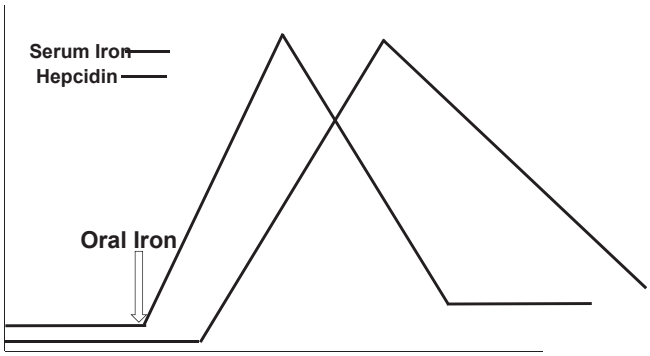
- Calcium, fiber can block iron absorption
  - Overcome by vitamin C
- Tea decreases 75-80%
- Coffee decreases 60% (5 oz!)



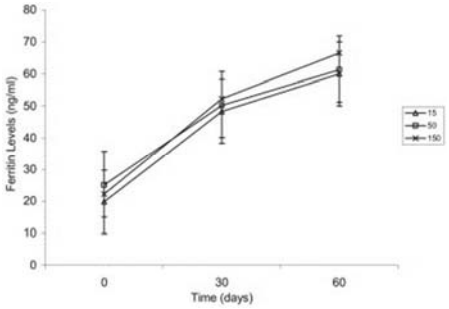
Oral Iron Pills

- Gut can only absorb a limited amount of iron
- Maxed out at ~ 10mg

Hepcidin Response to Iron



15 vs 50 vs 150mg Oral Iron



Am J Med. 2005 Oct;118(10):1142-7.

What I Do

- Cheapest iron pill
  - Ferrous sulfate
- Once a day with meals
  - Vitamin C 500
  - No tea or coffee
- If intolerant can try lower dose or every other day dosing

Response to Oral Iron

- Increased retic 7-10 days
- Increased Hgb 2 weeks
  - < 1g/dl predicts failure of oral iron
- Normalized 2 months

Parental Iron Therapy

- When to use
  - Refractory to oral iron
  - Unable to take oral iron
  - Cannot keep up with blood loss
    - Bariatric surgery
    - Inflammatory bowel disease
    - Chronic GI bleeding

IV Iron: Preparations

- Iron MW Iron Dextran: INFeD
- Iron Sucrose: Venofer
- Iron Gluconate: Ferrlecit
- Ferumoxytol: FeraHeme
- Ferric carboxymaltose: Injectafer
- Iron Isomaltose: Monofer

Dosing

- Iron dextran: 1-3 grams at once
- Venofer: 2-300 mg/day
- Ferrlecit: 250mg/day
- FeraHeme: 510 -1020mg mg/day
- Injectafer: 750mg/day
- Monofer: 1000mg/day

Dosing IV Iron

- Replacement formulas inaccurate
- Give 1000mg
  - Recheck in 4 weeks
  - If severe anemia recheck in two weeks

Safety

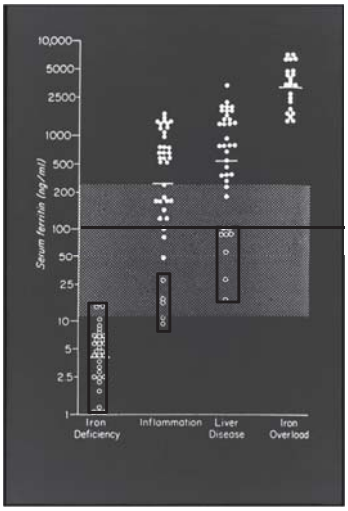
- Minor infusion reactions common (~1-2%) but true anaphylaxis very rare
- Death rates (per 100,000)
  - INFeD 0.8 (0-1.9)
  - Ferrlecit 6.3 (1.311.4)
  - Venofer 6.6 (3.1-9)
  - FeraHeme 3.5 (0-7.8)

Reactions

- Complement mediated pseudo-allergy
- Drug non-specific activated complement
  - Similar to rituximab etc.
- True anaphylaxis very rare
  - Negative tryptase > 200 reactions

Implication

- No value test dose
- Premedication often doesn't help
- Diphenhydramine makes things worse
- Treat as infusion reaction not allergy
- Studies show risk same with all iron preparations

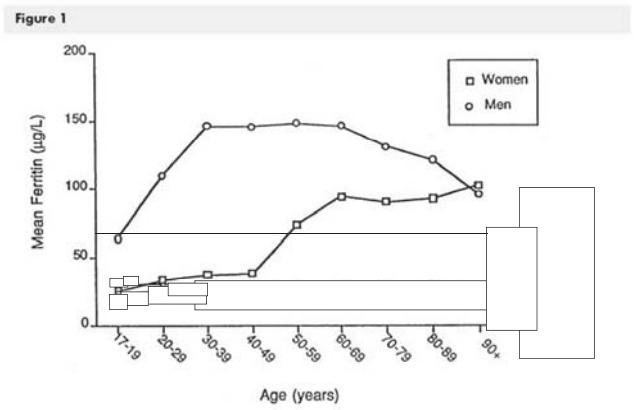


N Engl J Med. 1974 May 30;290(22):1213-6.

Iron Deficiency

- Serum ferritin is <u>BEST</u> non-invasive test of iron status
  - > 100 ng/mL rules out iron deficiency
  - Lower limit changes with age and condition
    - Patient over 65 with ferritin < 50 ng/mL <u>all</u> iron deficient

Age and Ferritin



Contributors to Iron Deficiency

- GI
  - NSAIA 10-15%
  - Colon Ca 5-10%
  - Gastric Ca 5%
  - Ulcers 5%
  - Angiodysplasia 5%
  - Esophagitis 2-4%
  - Esophageal Ca 1-2%
- Non-GI
  - Menstruation 20-30%
  - Celiac disease 4-6%
  - Bariatric surgery 1%

Iron Deficiency: GI Evaluation

- Most patients with identifiable source of GI blood loss
- Very high number with tumors
- Most common cause of missed cancer diagnosis
- Who *not* to evaluate?

GI Work-Up

- Iron deficiency anemia
  - Men with ferritins < 100 ng/mL
  - Post-menopausal women < 50 ng/mL (?100)
  - Women > 40
- Refractory iron deficiency
- Iron deficiency and GI symptoms

Bottom Line

- Too much iron
  - Most high ferritins not iron overload
  - T2*MRI
- Too little iron
  - Ferritins > 50 ng/mL are good
  - Oral iron
    - One pill/day
    - With vitamin C
    - With meat if feasible

Food Talk: What Your Patients Don't Tell You and Why You Need to Ask

Diane Stadler, PhD, RDN, LD

Slides not provided

DISCLOSURE

Relevant Financial Relationship(s)

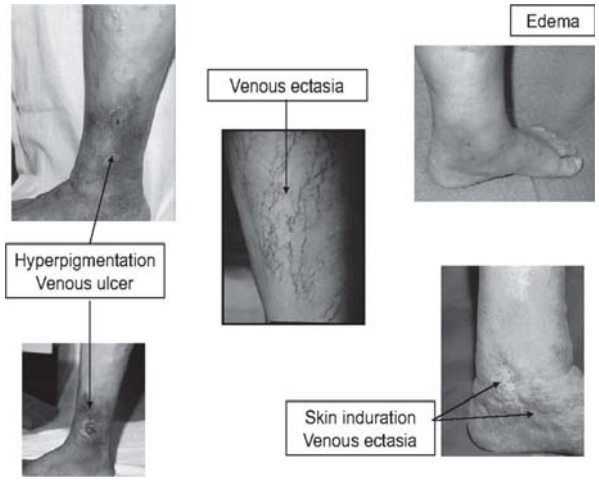
None

Why Prevent DVT?

- **Prevent post-phlebitic syndrome**
- **Prevent pulmonary embolism**
- **Prevent death**
- **Regulatory compliance**

Postphlebitic Syndrome

- **Five years after THR**
  - **11 patients with *asymptomatic* DVT**
  - **9/11 develop post-phlebitic syndrome**
    - **6 disabled**
    - **2 worse off**
  - **3/34 without DVT developed PPS**
  - **Acta Orthop Scand. 1994 Dec;65(6):595-8.**
- **30-50% of asymptomatic DVT develop PPS**

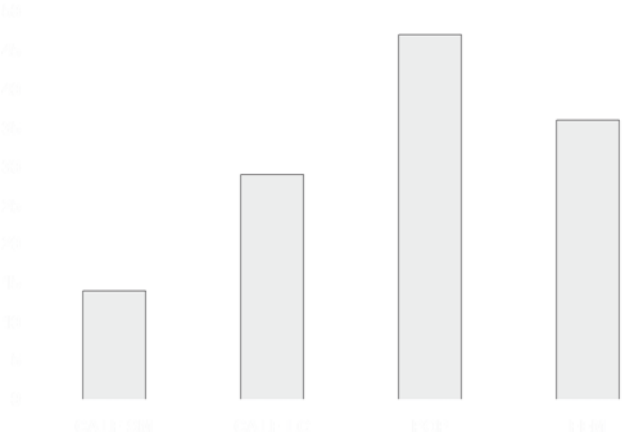


Blood, 19 November 2009, Vol. 114:4624-4631.

Calf Vein Thrombosis

- **Wide spread belief that CVT is trivial**
- **25% with late pulmonary emboli**
- **17 - 30% risk of progression**
- **RCT show benefits of treatment**

Risk of PE vs Site of Clot



Methods

- Intermittent pneumatic compression
- Aspirin
- IVC filters
- Low dose heparin
- Adjusted dose heparin
- Warfarin
- LMWH heparin
- Fondaparinux
- Direct oral Anticoagulants

Intermittent Pneumatic Compression

- Squeezes legs
  - Increases venous return
  - Stimulates fibrinolysis
- Not effective in preventing proximal thrombosis in highest risk patients
- Unlike drugs, effectiveness in DVT prevention NOT a requirement for IPC approval

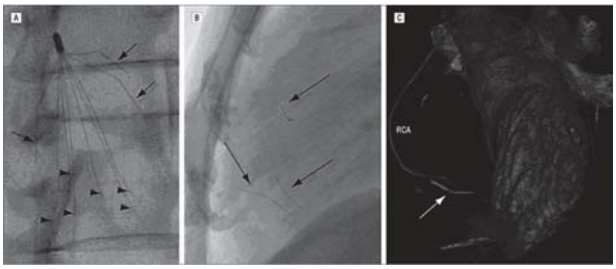
Intermittent Pneumatic Compression

- Good
  - Lower risk of bleeding
  - Effective
- Bad
  - Compliance mandatory
  - Not effective for highest risk patients
  - Not as effective for proximal vein thrombosis

IVC filters

- No good trials
- Fatal PE can still occur
- Does not prevent thrombosis
  - 2 most recent trials did not prevent PE!

Bard Recovery Vena Cava Filter



Nicholson, W. et al. Arch Intern Med 2010;170:1827-1831.

ARCHIVES OF INTERNAL MEDICINE

2019 Trauma Trial

- N = 240 trauma patients with contraindication to anticoagulation
- No difference in PE in filter vs no filter group

- N Engl J Med 2019; 381:328-337

IVC Filters

- Good
  - Effective if DVT present
- Bad
  - Raises risk of DVT
  - No good data
  - Not recommend for prophylaxis
    - May be harmful

Aspirin for Venous Disease

- Classically thought to be only for arterial disease
- But platelets do play a role in venous disease

Aspirin for DVT Prophylaxis

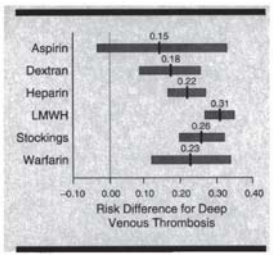
- Broad appeal
  - Cheap
  - Simple
- Wide spread use
- What is the data?

Early Trials

- Inconsistent data 1960-90
- Analysis of multiple trials and antiplatelet agents found ~ 30% risk reduction
  - Variable dose
  - Variable gender effect

Early Trials

- Meta-Analysis of aspirin restricted to trials with good design show no benefit
- JAMA 271:1780 1994



PEP Trial

- N = 13,356
- Aspirin 160mg vs placebo
- Other form of prophylaxis allowed
- Muddy endpoints
- Lancet 355:1295, 2000

PEP Trial

- Hip fracture
  - 29% risk reduction
  - Increased MI
  - Benefit seen after first week
- Hip/knee arthroplasty
  - No benefit
- 1.5% increase in major bleeds
- No large trials since
  - POISE-2 with no major benefit

Aspirin and Bleeding

- Aspirin is associated with a 2.2/100 excess rate of hematoma and infection
  - PEP 1.5/100 major bleeding
- Overall hematoma rates
  - Placebo: 5.6%
  - Aspirin: 7.8%
  - UFH: 6.0-6.2%
  - LMWH: 5.0-7.1%
- Arch Surg 141:790, BMJ: 1994; 308 : 235

One Potential Benefit

- PEP only showed benefit after a week
- Recent trial of rivaroxaban for 10 days and then rivaroxaban vs aspirin for the next 28 no difference in thrombosis
- N Engl J Med 2018; 378:699-707

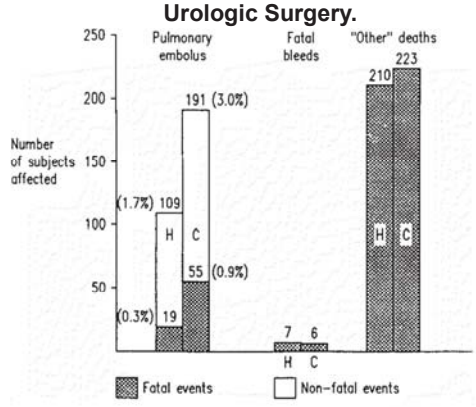
Aspirin: Bottom Line

- Inconsistent data
- No consistent dose
  - 160 – 3900mg/day
    - 80-200 mg best?
- Does raise risk of bleeding
- Low risk patients: mechanical effective
- High risk patients: more effective options
  - Aspirin an option after 7-10 of effective prophylaxis

Low Dose Heparin

- 5000 unit BID/TID before surgery
- Shown in the 70's to prevent PE death in general surgery patients
  - Findings in the 1980's extended to urology, orthopedics and GYN patients
- Bleeding risk increased for 3.8% to 5.9%
- Decreased risk of wound hematoma by injected away from wound site

All Available Data on Pulmonary Embolus and Mortality, from Evenly Randomized Trials of Perioperative Subcutaneous Heparin in General, Orthopedic, and Urologic Surgery.



Collins R et al. N Engl J Med 1988;318:1162-1173.

UFH

- Good
  - Effective
  - Cheap
- Bad
  - Not as effective in high risk patients
  - Time consuming
  - Heparin induced thrombocytopenia in 1% of patients

Warfarin

- Oldest method
- Effective in high risk patients
- Rate of hemorrhage varies with studies

Warfarin

- Day before or of surgery
- INR 2.0 by day 5, 2-3 after
- Two step
  - 5-14 days pre-op INR 1.5
  - INR 2-3 after surgery

Warfarin

- Good
  - Effective in high risk patients
  - Easy to do long term therapy
  - Well known drug
- Bad
  - Not very flexible
  - Difficult to control
  - Need good monitoring

LMWH Heparin

- Standard heparin is mixture of chains of complex sugars of varying length
- UFH is treated to make LMWH heparin
- Multiple brands

LMWH Heparin

- Same or better than UFH or warfarin in patients
  - LMWH more effective in higher risk patients
  - Much less incidence of HIT

LMWH

- Good
  - Very effective
  - Less HIT
- Bad
  - Slightly increase risk of bleeding
  - Cost
  - Injection

New Drugs

- Rivaroxaban
- Dabigatran
- Apixaban

Rivaroxaban

- Oral Xa Inhibitor
- Bioavailability: 80-100%
- Onset of action: 2.5-4 hours
- Half-life : 5-9 hours
- Renal excretion: ~66%
- Drug interactions: CYP 3A4

DVT Prevention

- Rivaroxaban 10mg qDay
- THR vs 40mg of enoxaparin (N = 4435)
  - Decreased proximal DVT (0.1 vs 2.0%)
  - No increase risk of bleeding
  - N Engl J Med. 2008 358:2765-75.
- TKR vs 40mg of enoxaparin (N= 2439)
  - Decrease proximal (1.1 vs 2.3%) and symptomatic DVT (0.7 vs 2.0%)
  - No increase risk of bleeding
  - N Engl J Med. 2008 358:2776-86

Apixaban

- Oral Xa Inhibitor
- Bioavailability: 66%
- Onset of action: 1-3 hours
- Half-life : 8-15 hours
- Renal excretion: 25%
- Drug interactions: CYP 3A4
  - Multiple other pathways

DVT Prevention

- Apixaban 2.5mg bid
- THR vs 40mg of enoxaparin (N = 1949)
  - Decreased proximal DVT (0.3 vs 0.9%)
  - No increase risk of bleeding
  - N Engl J Med. 2010 363:2487-98
- TKR vs 40mg of enoxaparin (N= 3057)
  - Decrease proximal DVT (0.76 vs 2.2%)
  - No increase risk of bleeding
  - Lancet 2010 375:807-15

Joint Replacement

Drug	Thrombosis	Bleeding
Apixaban	Better	Equal
Dabigatran	Equal	Equal
Rivaroxaban	Better	Equal

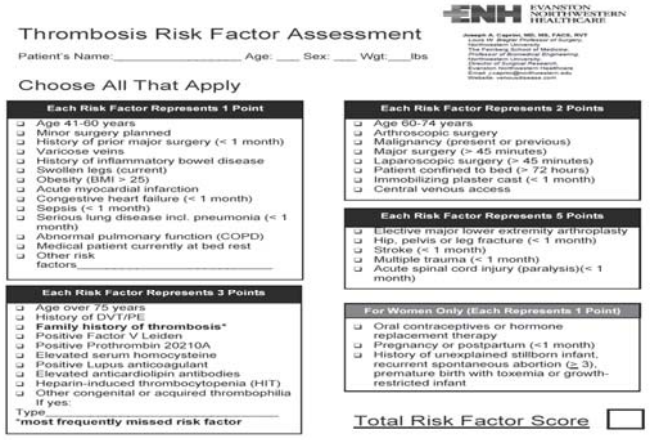
Prophylaxis

- All three agents effective
- Rivaroxaban approved
  - Oral and cheaper!
- Apixaban also approved

DVT Prophylaxis: Doing it Right!

- Assessing patients risk
- Matching prophylaxis for risk

VTE Risk Stratification Example



ENH EVANSTON NORTHWESTERN HEALTHCARE

Thrombosis Risk Factor Assessment

Patient's Name:_____ Age: ___ Sex: ___ Wgt:___lbs

Choose All That Apply

Each Risk Factor Represents 1 Point

- ☐ Age 41-60 years
- ☐ Minor surgery planned
- ☐ History of prior major surgery (< 1 month)
- ☐ Varicose veins
- ☐ History of inflammatory bowel disease
- ☐ Swollen legs (current)
- ☐ Obesity (BMI > 25)
- ☐ Acute myocardial infarction
- ☐ Congestive heart failure (< 1 month)
- ☐ Sepsis (< 1 month)
- ☐ Serious lung disease incl. pneumonia (< 1 month)
- ☐ Abnormal pulmonary function (COPD)
- ☐ Medical patient currently at bed rest
- ☐ Other risk factors_____

Each Risk Factor Represents 2 Points

- ☐ Age 60-74 years
- ☐ Arthroscopic surgery
- ☐ Malignancy (present or previous)
- ☐ Major surgery (> 45 minutes)
- ☐ Laparoscopic surgery (> 45 minutes)
- ☐ Patient confined to bed (> 72 hours)
- ☐ Immobilizing plaster cast (< 1 month)
- ☐ Central venous access

Each Risk Factor Represents 3 Points

- ☐ Age over 75 years
- ☐ History of DVT/PE
- ☐ **Family history of thrombosis***
- ☐ Positive Factor V Leiden
- ☐ Positive Prothrombin 20210A
- ☐ Elevated serum homocysteine
- ☐ Positive Lupus anticoagulant
- ☐ Elevated anticardiolipin antibodies
- ☐ Heparin-induced thrombocytopenia (HIT)
- ☐ Other congenital or acquired thrombophilia

If yes:

Type_____

***most frequently missed risk factor**

Each Risk Factor Represents 5 Points

- ☐ Elective major lower extremity arthroplasty
- ☐ Hip, pelvis or leg fracture (< 1 month)
- ☐ Stroke (< 1 month)
- ☐ Multiple trauma (< 1 month)
- ☐ Acute spinal cord injury (paralysis)(< 1 month)

For Women Only (Each Represents 1 Point)

- ☐ Oral contraceptives or hormone replacement therapy
- ☐ Pregnancy or postpartum (<1 month)
- ☐ History of unexplained stillborn infant, recurrent spontaneous abortion (≥ 3), premature birth with toxemia or growth-restricted infant

Total Risk Factor Score ☐

Caprini et.al.

Scores

- Score 0-1: Low risk of VTE
- Score 2: Moderate of VTE
- Score 3-4: High risk of VTE
- Score ≥ 5: Highest risk for VTE

Assessing Risk

- Low risk: minor surgery, <40
- Moderate risk: surgery >40
- High risk: hx DVT/PE, hypercoagulable state, cancer, THR/TKR, trauma

Assessing Risk

	CVT	PVT	PE	Death
Low	2	0.4	0.3	0.002
Mod	20-40	4-8	2-4	0.4-1.0
Highest	40-80	4-10	4-10	0.5-5

Low Risk Patients

- Younger than 40, uncomplicated surgery, no OCP, no cancer
  - Calf vein thrombosis 2%
  - Prox vein thrombosis 0.4%
  - Fatal PE < 0.02%
- Rx: early ambulation

Medium Risk Patients

- General surgery in patients >40, IM patients, routine medical patients
  - Calf vein thrombosis 10 - 20%
  - Prox vein thrombosis 2 - 4%
  - Fatal PE 0.2 - 0.5%
- Rx: LDH, IPC, LMWH

High Risk Patients

- Orthopedic surgery, previous DVT, cancer, complex medical patients, ICU
  - Calf vein thrombosis 40 - 70%
  - Proximal vein thrombosis 10 - 20%
  - Fatal PE 1 - 5%
- Rx: LMWH, fondaparinux, warfarin, direct oral anticoagulants

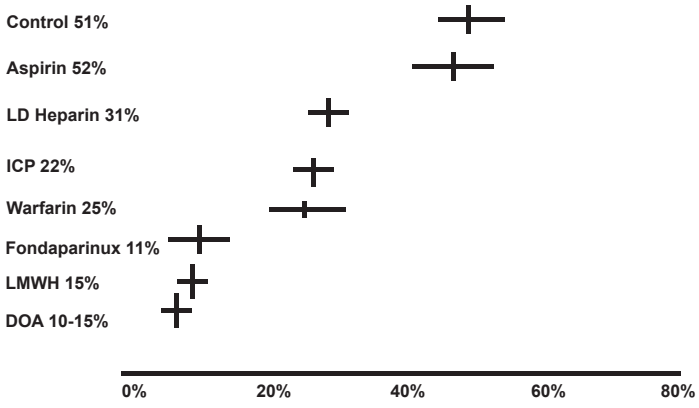
Hip Replacement

- High risk
- DVT rate 50%, 20% proximal, 1-2% fatal
- Decreasing death rates over time
- High incidence of isolated femoral vein thrombosis

Hip Replacement

- UFH, IPC not optimal therapy
- Warfarin
- LMWH heparin
- Fondaparinux
- Direct oral anticoagulants

Hip Replacement



Knee Replacement

- Rate of calf vein DVT high
- Low incidence of PE except in bilateral procedures
- IPC
- Warfarin
- LMWH heparin
- Fondaparinux
- Direct oral anticoagulants

Arthroscopy

- Low rates of thrombosis
- No prophylaxis unless risk factors
- Rivaroxaban x 7 days

Hip Fracture

- 10% of patients with DVT <u>before</u> surgery
- DVT 50 - 80%, PE 10-20%, fatal 5-7%
- Warfarin reduced fatal PE from 7% to 1%
- Fondaparinux
- LMWH heparin

Cancer

- Major risk factor
- Consistently raises risk of thrombosis at least 3 fold
- Leading cause of death after cancer surgery
- Reasons
  - Tumor procoagulants
  - Chemotherapy
  - Surgery
  - Catheters (15-50%)

Cancer

- Cancers with highest risk
  - GI cancers
  - Brain tumors
  - Lung cancer

Oncological Surgery

- Abdomen - DVT increased 3 fold over benign surgery
- Brain surgery - rates may be as high at 60%
- GYN oncology - 2-3 fold increase over benign procedures
- LMWH or fondaparinux

Trauma

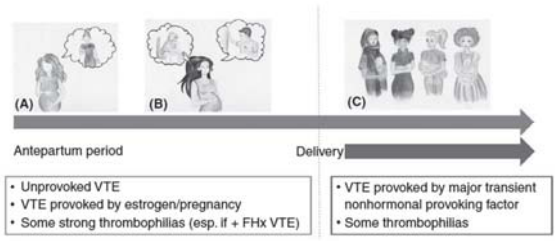
- All trauma increases the risk of DVT
- Disrupts all Virchow's triad
- Risk even for young patients
- LMWH standard

Obesity

- Amazingly no consensus!
- 0.5 mg/kg LMWH daily
- BMI mg/LMWH daily
- 40mg bid > 40 BMI

Pregnancy

- Provoked thrombosis
  - Post-partum x 6 week
- Estrogen provoked
  - Pre and post partum
- Idiopathic thrombosis
  - Pre and post partum
- Thrombophilia
  - Low risk: post partum
  - High risk: pre and post partum



- Pre partum
  - LMWH 40mg daily
- Post
  - LMWH 40mg daily
  - Rivaroxaban 10mg daily
    - Contraindicated if breast feeding

Medical Patients

- Universal prophylaxis remains controversial!
- Range of patients in hospital
- Risk scoring recommended
  - Simple
  - Padua

Table 2. Padua Prediction Score Risk Assessment Model[a]

Baseline Features	Score[b]
Active cancer[c]	3
Previous VTE (excludes superficial vein thrombosis)	3
Reduced mobility[d]	3
Already known thrombophilic condition[e]	3
Recent (≤1 month) trauma and/or surgery	2
Elderly age (≥70 years)	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI ≥30 kg/m²)	1
Ongoing hormonal treatment	1

Abbreviations: BMI, body mass index; VTE, venous thromboembolism.

[a]This table is based on information in reference 21 in the citation list.
[b]A total score ≥4 indicates a high risk of VTE.
[c]Includes patients with local or distant metastases and/or in whom chemotherapy or radiotherapy had been performed in the previous 6 months.
[d]Includes bed rest with bathroom privileges for at least 3 days (due to patient's limitations or per physician's orders).
[e]Includes carriage of defects of antithrombin, protein C, or protein S, or presence of factor V Leiden, antiphospholipid syndrome, or G20210A prothrombin mutations.

Padua Score

- 4 or more high risk
- Accounts for range of illness
- Limited verification

Assessing Risk: Medical Patients

- Low risk: minor illness, <40 (with no risk factors)
- Moderate risk: Age > 40, bed rest > 3 days
- High risk: hx DVT/PE, cancer, inflammatory bowel disease, recent MI, stroke, ICU admission

Choices

- UFH
  - Simple
  - Controversial BID vs TID
- Enoxaparin
  - Less HIT
  - Less work for nurses
  - $$$

Why is DVT Prophylaxis Underused?

- Fear of bleeding
  - Wound complications
  - Need for transfusion
  - Need for re-operations
  - Fatal outcomes

Is this fear justified?

Meta-Analysis

- 33 RCT trials of prophylaxis
- N = 33,813 patients
- Examined 8 complications

Table 3. Complication Rates by Type of Complication

Type of Complication	No. of RCTs	Sample Size of Potential Patients: Pharmacologic Prophylaxis Group	Sample Size of Potential Patients: Control Group	Complications, Mean (Range), %: LMW Heparin Group: High	LMW Heparin Group: Low	LDU Heparin Group: High	LDU Heparin Group: Low	Total Pharmacologic Prophylaxis Group	Control Group
Injection site bruising	18	13574	359	3.4 (1.1-7.1)	6.8 (0.5-16.3)	8.3 (2.0-20.0)	8.3 (0.6-15.7)	6.9 (0.7-20.2)	2.8 (0-7.6)
Wound hematoma	26	26371	854	4.0 (0-8.6)	6.6 (0-9.1)	5.5 (0-9.2)	4.2 (0.6-19.0)	5.7 (0-19.0)	0.8 (0-3.2)
Drain site bleeding	5	5307	169	1.8 (2.1-3.0)	2.0 (0.6-5.2)	0.4 (0.4)	2.8 (1.2-6.1)	2.0 (0.6-5.6)	0.6 (0.6)
Hematuria	7	15406	NA	5.8 (0.2-10.0)	0.4 (0-0.5)	4.7 (0.3-9.6)	0.2 (0.2)	1.6 (0.2-9.8)	NA
GI tract bleeding	6	12928	52	1.0 (1.0)	<0.1 (0.04-0.3)	0.4 (0.4)	0.5 (0-1.0)	0.2 (0.04-2.5)	1.9 (1.9)
RP bleeding	3	12642	NA	0.3 (0.4)	<0.1 (0.03-0.1)	0.4 (0.4)	0.2 (0.2)	<0.1 (0.03-0.3)	NA
Discontinue prophylaxis	12	10540	NA	2.0 (1.5-5.0)	1.7 (0.9-2.3)	3.3 (2.1-5.0)	1.9 (0-7.1)	2.0 (0-7.1)	NA
Subsequent operation	9	20618	822	1.0 (0.4-1.5)	0.5 (0.2-1.0)	1.8 (1.8)	1.0 (0.2-1.7)	0.7 (0.3-1.3)	0.7 (0.6-0.8)

Abbreviations: GI, gastrointestinal; LDU, low-dose unfractionated; LMW, low-molecular-weight; NA, data not available; RCT, randomized controlled trial; RP, retroperitoneal.

Leonardi, M. J. et al. Arch Surg 2006;141:790-799.

Findings

- **Major Bleeding**
  - **GI 0.2%**
  - **Retroperitoneal < 0.1%**
- **Reoperation - < 1%**
- **Need to stop prophylaxis 2%**

How to Get it Done: I

- **One clear and simple set of guidelines**
- **Pre-printed admit orders**
  - **Need to put something in prophylaxis line**
- **Recovery room**
  - **Cannot leave recovery room without orders filled out**

Oregon Health & Science University Hospitals and Clinics Provider's Orders

VENOUS THROMBOEMBOLISM (VTE) RISK ASSESSMENT AND PROPHYLAXIS ORDERS FOR ADULT SURGICAL INPATIENTS

Page 1 of 1

Date: Time: Weight: kg (required for pts > 80 kg)

1. Allergies: Drug / Reaction:
Other / Reaction:

2. VTE Risk Assessment: Mark patient's risk category

Low Risk	Moderate Risk	High Risk

• Age < 40
• Minor Surgery
• No additional Risk Factors
• In house < 24 hrs
	• Age 40-60; No additional Risk Factors
	• Minor Surgery with additional Risk Factors
	• Risk Factors (for example):
	  • Prior VTE
	  • Active Cancer
	  • Known Hypercoagulable Condition
		• Age > 60
		• Age 40-60 with additional Risk Factors
		• Hip or Knee Arthroplasty
		• Hip Fracture
		• Major Trauma
		• Spinal Cord Injury

3. VTE Ppx Contraindications: checking 1 or more boxes indicates contraindication
☐ Thrombocytopenia (platelets < 50,000) ☐ Known bleeding risk
☐ Liver failure with elevated INR (≥ 1.5) ☐ Heparin or warfarin in patient with HIT
☐ Uncontrolled hypertension (SBP > 200, DBP > 110) ☐ Other

4. VTE Prophylaxis Considerations
Neuraxial Catheter (Epidural/intrathecal): The only approved LMWH prophylaxis option with neuraxial catheters is enoxaparin 40 mg subcut q day. Currently use of fondaparinux is contraindicated in these pts.
Timing of Prophylaxis: Enoxaparin, fondaparinux, or warfarin should be started within 12 hours after surgery. Initiation of medical prophylaxis may be delayed until 24 hrs (or more) after surgery if the surgeon deems the patient to be at high risk for bleeding.
Renal Failure: In patients with renal failure, the dose of enoxaparin should be decreased by 50%. (e.g. 40 mg q day → 20 mg q day, 30 mg BID → 30 mg q day)

5. VTE Prophylaxis Orders: Start Date

Low Risk	• Early ambulation, per post-op activity order	
Moderate Risk	• Sequential compression device (SCD); and/or	☐ Heparin 5,000 units subcut q 8 hrs (Check platelets on Day 1 and QOD from Day 4-14) ☐ Heparin 5,000 units subcut q 12 hrs (Check platelets on Day 1 and QOD from Day 4-14) ☐ Enoxaparin 40 mg subcut q day (renal impairment, see below*)
High Risk	• Sequential compression device (SCD); and	☐ Enoxaparin 40 mg subcut q day (renal impairment, see below*) ☐ Enoxaparin 30 mg subcut BID (renal impairment, see below*) ☐ Fondaparinux 2.5 mg subcut q day (contraindicated in renal failure) ☐ Warfarin mg po q day at 2100 (suggested starting dose is 5 mg, adjust to achieve goal INR 2-3)

*Renal impairment pts (CrCl < 30 mL/min) dose adjustment: ☐ Enoxaparin 20 mg subcut q day ☐ Enoxaparin 30 mg subcut q day

☐ SCD only due to contraindications listed above or

I certify that all orders (pg 1 of 1) are in effect as designated by ☑ or as written in, unless crossed out.

Provider's Signature Provider's Pager #

ONLINE 3/2007 PO-7272

How to Get it Done: II EMR Era

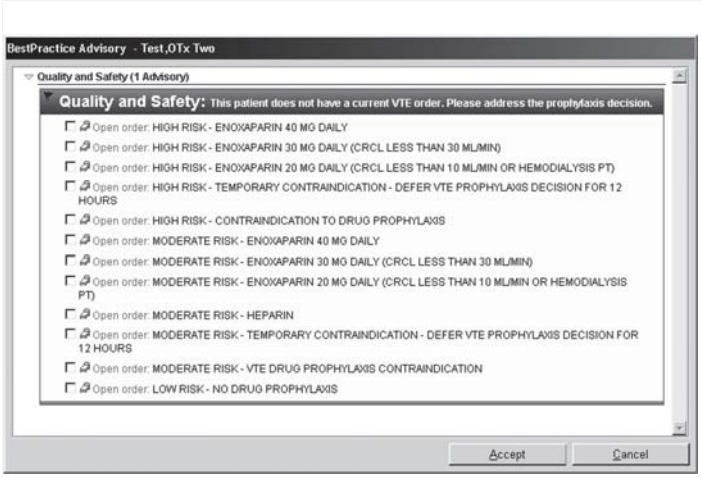
- **Pro**
  - **Automatic reminders**
  - **Order sets**
- **Con**
  - **Over prophylaxis**
  - **Lack of flexibility**

Automatic Reminders

- **Pop-up reminders**
  - **Admission**
  - **After surgery**
  - **After 24 hours**
  - **In patients with no orders**

Order Sets

- Automatic part of admit or post-operative orders



Over Prophylaxis

- Blind clicking or fixed order sets can lead to prophylaxing:
  - Bleeding patients
  - Patients with contraindications
  - Patients already anticoagulated

Lack of Flexibility

Struggle between simple orders and individualizing for each patients

Screening

- Screening patients for DVT not recommended
- But performed in many institutions
  - Increase venous thrombosis
  - No change in PE

What is a Bad DVT?

- Upper extremity?
- Line related?
- Superficial thrombophlebitis?
- Calf?

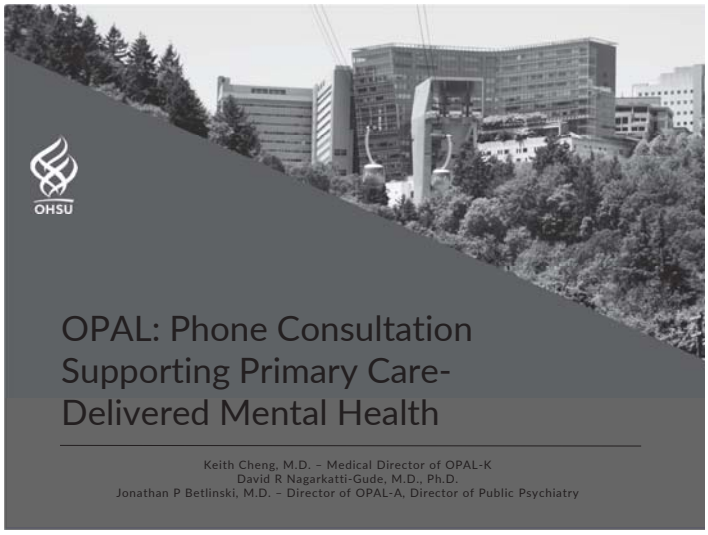
Take Home Points

- **Preventing thrombosis is good!**
  - **Prevents death**
  - **Prevents long term disability**
- **Execution can be difficult**
  - **Scoring system**
  - **Provider buy in**
  - **Make automatic**
  - **Simplicity!**

The Impact of an Oral Health Integration Training on Children's Receipt of Oral Health and Dental Services

Hannah Cohen-Cline, PhD, MPH

Slides not provided

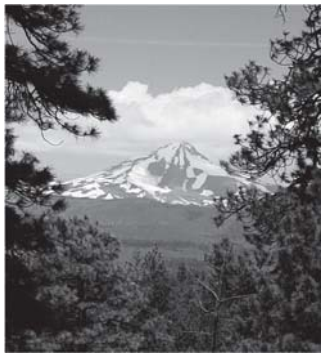


OPAL: Phone Consultation Supporting Primary Care-Delivered Mental Health

Keith Cheng, M.D. – Medical Director of OPAL-K
David R Nagarkatti-Gude, M.D., Ph.D.
Jonathan P Betlinski, M.D. – Director of OPAL-A, Director of Public Psychiatry

Disclosures

We have no conflicts of interest or other disclosures



Mt. Jefferson

Some OPAL History

Oregon Coast

Collaboration (2006)

- Oregon Council of Child and Adolescent Psychiatry (OCCAP)
- Oregon Pediatric Society (OPS)
- Oregon Family Support Network (OFSN)

OPAL-K Beginnings

- The 2013 Legislative's New Investments in Child and Young Adult MH/CD Services
- OHSU Division of Child and Adolescent Psychiatry funded in January of 2014
  - Consultation: Massachusetts MCPAP and Psychiatric Access Line (PAL) at the University of Washington
  - Collaboration with Oregon Pediatric Society
  - Began taking calls in June 2014 (pilot with Central Oregon Pediatric Associates (COPA) in Bend)
  - Statewide in July 2014

Goals of OPAL-K

- Increase the number of children who receive treatment for their mental health challenges
- Decrease delays in treatment
- Target appropriate level of intervention
- Utilize a "biopsychosocialecodevelopmental" framework
- Improve appropriate prescribing of psychotropic medications

Goals Continued….

- Create opportunities for consultation mentoring and education,
- Create a service that is blind to insurance and statewide for the care of all youth in Oregon
- Improve appropriate prescribing of psychotropic medications generally and with a particular focus on youth in foster care.

Basics

- Hours of operation 9-5 Monday- Friday
- Closed on national holidays
- PCPs call the OPAL office (already enrolled or will enroll at the time)
- Enter the patient's demographics (Name, DOB, Insurance, foster care experience)
- Call is transferred to on call psychiatrist
- Consultant writes a summary
- Office staff will send the summary via fax or secure email

Call Summary Outline

- Reason for Consultation
- Medication Management Considerations
- Monitoring Ideas
- Psychosocial treatment advice
- Other Comments
- Suggested Care Guides

Total PCP Consult Calls

• OPAL-K	(June 2014- January 2020)	3,358	calls
• OPAL-A	(October 2018-January 2020)	744	calls
• Foster Care	(June 2014- October 2019)	266	calls
• Pharmacy reviews	(Aug 2019 January 2020)	76	calls

OPAL-K Spinoffs

- OPAL-K Foster Care Psychtropic Medication Monitoring Program
- OHA Pharmacy Antipsychotic Project
- OPAL-K Suicidal Ideations Monitoring Project
- OPAL-K Increasing Trauma monitoring

Deschutes River

OPAL-K/OHA Pharmacy Project

Project Aims

- Identify risk cases
- Provide Phone Consultation
- Decrease inappropriate Prescribing
- Increase Metabolic Screening
- Improve Better Documentation

Exclusion Criteria

- Patients with a history of long-term antipsychotic use > 9 months of covered days in the past year; (ideally want to target only new start patients who appear to be initiating long-term therapy)
- Any patient already referred to OPAL-K within the prior year (once the program is implemented)
- Patient who has been reviewed by OPAL-K via a different program (i.e., foster care profiles) in the prior year

Inclusion Criteria

- Patients age <10 years old
- Patients who have ≥90 covered days (in the last 6 months) for medications within the following PDL classes: antipsychotics, 2nd gen and antipsychotics, 1st gen
- All Medicaid cases not just foster care

High Priority Cases

- 6 months of more than one antipsychotic
- No metabolic testing
- No FDA indication

Moderate Priority

- 6 months of one antipsychotic
- No metabolic testing
- No FDA indication
- No claims for nonmedical treatments

Low Priority Cases

- Patients seen by psychiatrists
- Have FDA Approved indication
- Less than 6 months of treatment

Case Distribution

High - 23
Medium - 12
Low - 140

- Number of cases contacted = 64
- Number of cases that scheduled and received consultation = 35

Clinician Breakdown

- Psychiatrists (n=7) (n=7)
- Pediatricians/Family Practice (n=33) (n=15)
- Psych Nurse Practitioners (n=8) (n=4)
- FNP (n=13) (n=5)
- Physician Assistants (n=1) (n=0)
- No ID (n=2) (n=0)

Sample Case: polypharmacy

- 8 year old boy
- Dx:
  ADHD
  PTSD
  Separation Anxiety

Medication List:
1. guanfacine
2. clonidine
3. fluoxetine
4. atomoxetine
5. risperidone
6. dextroamphetamine

Better Documentation

- Balancing Test
- Consent
- No FDA indications
- Clinical Reasons for Off-label prescribing

Metolius River

OPAL-K
Foster Care Psychotropic Medication Monitoring Project

Some Foster Care Facts

- 2009 - 19.6% of foster care youth on psychotropics
- 2016 - 9.4% of foster care youth on psychotropics (n=8457)
- 2020 - Oregon has less than 8000 youth in care

Foster Care Consult Criteria

- Antipsychotic without FDA indication
- Polypharmacy 4 or more psychotropic meds
- Two or more meds in one class
- Doses greater than FDA approved maximum
- Psychotropics in youth younger than 6 years

Foster Care Data Analysis

- N = 746 controls, N = 88
- Off Label Antipsychotic prescriptions.
  Foster Care Youth > non Foster Care Youth
- 16% had no clear FDA approved indication
- Being male, having PTSD, & developmentally disabled, are most common risks for getting off-label antipsychotic treatment

Can primary care clinicians broaden their ROS when gathering mental health history as a result of using OPAL-K?

Painted Hills

Changing clinician mental health screening patterns through curbside consultation

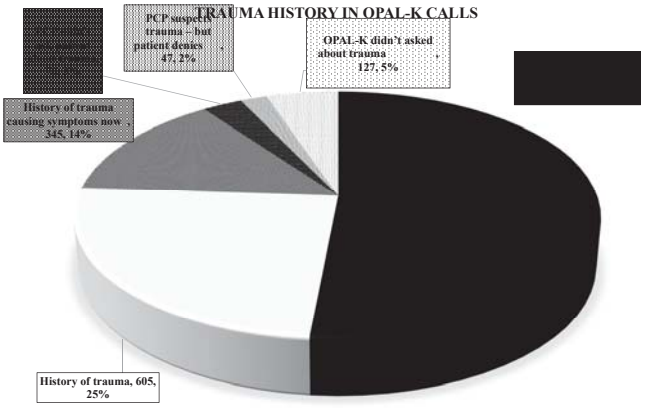
- Trauma data
- Suicide data

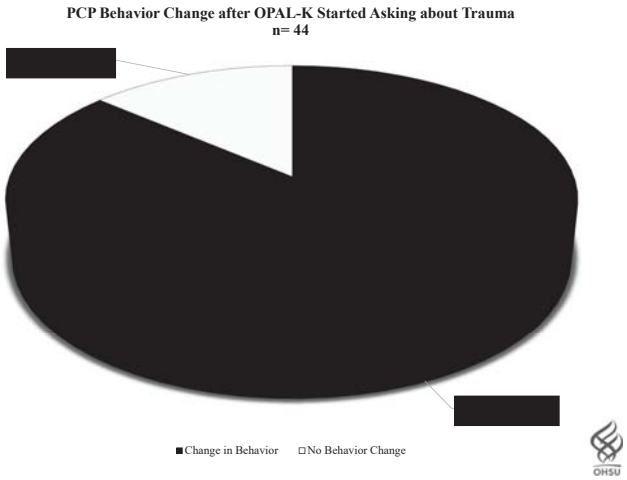
OPAL-K Increasing Trauma monitoring Project

Columbia Gorge

Trauma Prompt

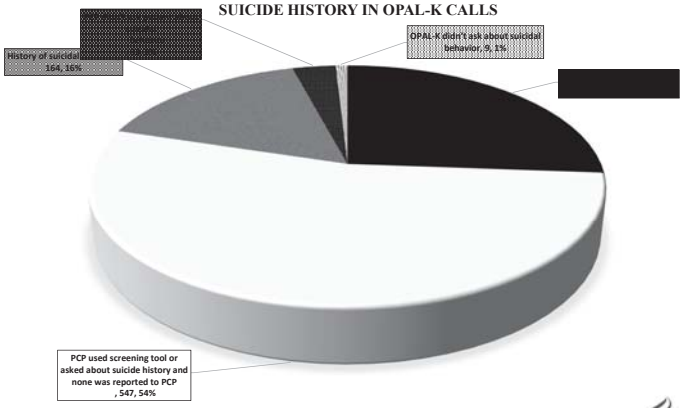
- OPAL-K targeted trauma screening for QI project
- Consultants should query about trauma in all calls
- “Do you think trauma has anything to do with the present mental health concerns?”

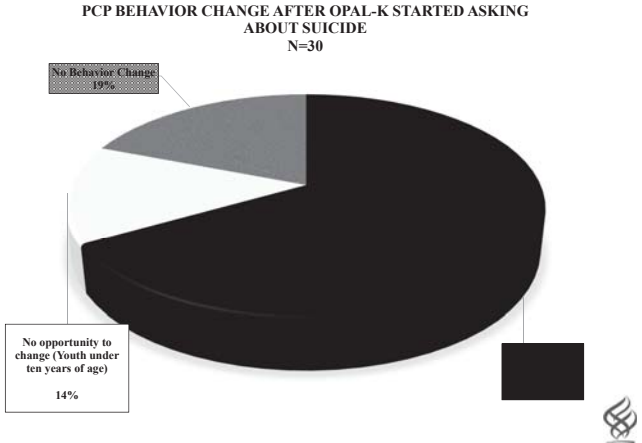




OPAL-K Suicidal Ideations Monitoring Project

Columbia Gorge





What's an OPAL call actually like?

Case #1: Outpatient treatment of bipolar disorder

- Hispanic male in his 30s
- Lives with supportive family
- CC: 2 days without sleep, rapid thoughts, ruminating
- Dx: schizophrenia vs bipolar disorder
- PMHx: obesity
- Tx: Lithium 300mg qam and 600mg qhs
- Recent tx: add Risperidone 1mg BID

OPAL writeup: Reason for consultation

Thank you for calling about your young male patient who lives with Bipolar disorder (previously stable on Lithium total daily dose of 900mg) who has experienced several days of inability to sleep, increased anxiety, rumination that are consistent with prior manic episodes. Lithium level is pending right now. You augmented with risperidone, which he took as 2mg HS (1mg dose was insufficient for sleep) and was beneficial for sleep but caused some daytime sedation. He's previously been treated with Zyprexa and reportedly did well with that medication, though his BMI is already in the obese range so metabolic side effects are a significant consideration for treatment choice for him. He lives with supportive family now. He is also concerned for anxiety, though it's unclear to what extent that increased anxiety is happening in the context of the current mood episode vs being an underlying and co-morbid condition.

Medications to consider:

- Check Lithium level:
  - ≦ 0.7: Increase Lithium to 600mg BID
  - 0.8-0.9: may increase Lithium to 600mg BID but monitor closely
  - 1.0+: maintain Lithium, modulate antipsychotic
    - Lower risperidone dose
    - Replace risperidone w/ aripiprazole or quetiapine

OPAL writeup: Medications to consider

I would make the next treatment step depending in part on the Lithium level.

- Li level 0.7 or below: Increase Lithium to 600mg BID

- Lithium level 0.8-0.9: May increase to Lithium 600mg BID, but will need to be very safe with observing for symptoms of Lithium toxicity and maintaining; depending on his ability to stay hydrated, dose consistently, and avoid meds that may increase Lithium level (e.g even OTC NSAIDs) it may not feel comfortable to increase

- Li 1.0+: don't increase; in general our goal Li level for acute mania is 0.8 - 1.2, then 0.7-1.0 for maintenance.

OPAL writeup: Medications to consider

If maintaining Lithium at current dose:
Step 1) **DECREASE Risperidone 2->1.5mg, monitoring for improved sleep without daytime sedation**

Step 2 options) **Cross-taper off Risperidone to alternate antipsychotic** (e.g risperidone 1mg + Abilify 5mg or Quetiapine 50mg, then risperidone 0.5mg + Abilify 10mg or Quetiapine 100mg)

***If priority is to avoid daytime sedation, avoid metabolic risks**: Abilify 5mg x3days, then 10mg x3days, then 15mg
***If priority is to avoid akathisia, or maximize sedation and rapid acting:** Quetiapine 50mg qhs. Increase by 50mg q1-7 days as tolerated (primarily risks of sedation, orthostatic hypotension) with goal of 400mg in mind (okay if plateaus helpful at lower dose since giving concurrently with Lithium)

OPAL writeup: Medications to consider

***Possible augmentation**, particularly if waiting for slower Abilify to reach target dose and take effect: - Lorazepam 0.5-1mg BID PRN anxiety, insomnia. Would caution this as a bridge medication only, though reasonable to continue for weeks to a few months to achieve mood stability

***If akathisia present** - may consider switching to lower akathisia risk medication (e.g Quetiapine) or alternatively if antipsychotic is otherwise helpful can trial Propranolol 10-30mg BID to treat akathisia

OPAL writeup: Suggestions for monitoring

You discussed the most important elements for monitoring your patient. The following **scales may be helpful to monitor mood symptoms** over time and gauge response to treatment:

- Patients can rate mania symptoms using **Altman Self-Mania Rating Scale** (http://www.cqaimh.org/pdf/tool_asrm.pdf) AND/OR
- Clinicians can rate mania symptoms using **Young Mania Rating Scale** (https://www.outcometracker.org/library/YMRS.pdf)

- **Barnes Akathisia rating Scale** (https://outcometracker.org/library/BAS.pdf) can help gauge presence of akathisia, and respond to treatment if present

- Kathryn Zeier et al have a good summary for lab monitoring in a patient taking chronic antipsychotic treatment

OPAL writeup: Non-medication interventions

I agree with **referral for local mental health services**, as this may be the best way to treat his anxiety once it's more clear what that anxiety entails. That would also hopefully give more opportunity for his **family to learn more** about the condition and be able to help him with monitoring symptoms of Bipolar disorder as well as potential medication-related symptoms.

OPAL writeup: Other comments

Thank you for providing excellent care for this patient, please feel free to call back with further questions about this patient or anybody else to whom you provide care!

Case #2: Treatment-refractory insomnia

- Woman in her 50s
- CC: insomnia (onset and maintenance), trazodone side effects
- Dx: complex PTSD
- PMHx: DM2 (poorly controlled)
- Tx: fluoxetine, buspirone, trazodone
- Prior meds: prazosin, benzodiazepines, zolpidem, quetiapine

OPAL writeup: Reason for consultation

Thank you for calling about your middle-aged Female with a history of complex PTSD. She has been under your great care for several years and she is awaiting referral to a psychiatrist. She was psychiatrically hospitalized in November 2019 and was discharged on fluoxetine, buspirone and trazodone. Since then she is struggling with insomnia, both initial and maintaining sleep, and finds that trazodone makes her feel agitated at bedtime and results in sedation and sluggishness the next morning. She is hoping to switch agents.

In the past, she has tried prazosin which was initially effective then effect stopped, benzodiazepines which caused dissociation, zolpidem which caused paranoia and SI and quetiapine which was effective at 50mg. She does have poorly controlled type II diabetes and you are rightfully concerned about restarting quetiapine.

OPAL writeup: Medications to consider

We discussed various options for managing insomnia in this patient. I agree completely with you in **avoiding benzodiazpines and antipsychotics if at all possible**. Many other options are possible.

First, we discussed her prior **prazosin** trial. Studies have indicated efficacy at doses between 1-20mg and it may be worthwhile to **re-trial** this medication and increase to efficacy as long as her blood pressure tolerates the medication. It is particularly helpful for nightmares and hypervigilance associated with trauma-related disorders.

OPAL writeup: Medications to consider

We also discussed the various agents that are currently recommended for treatment of sleep onset and sleep maintenance insomnia, with a particular focus on ramelteon in this patient. Given her sensitivity to "z-drugs" (zolpidem, eszopiclone (Lunesta), zaleplon (Sonata), I would **consider ramelteon first** given it's lower risks and side effect profile. Ramelteon has been shown to be most effective in sleep onset insomnia and has been shown that benefits outweigh harms. It is a melatonin receptor 1 and 2 agonist and is not associated with tolerance or withdrawal and does not carry risk in overdose. One thing to know is that while 8mg is the usual prescribed dose, some patients may require higher doses up to 64mg. There have been no safety or tolerability concerns up to 160mg.

An excellent review article on the pharmacologic management of chronic insomnia in adults (containing an excellent chart for quick reference) can be found here:

OPAL writeup: Suggestions for monitoring

Continue to track mood symptoms as you've been doing. **PCL-C** can also be a useful tool in tracking PTSD symptoms over time.

OPAL writeup: Non-medication interventions

Continue communication and **collaboration with the patient's trauma therapist**. Great job in connecting her to such an important resource!

OPAL writeup: Other comments

Thank you for sharing this case. Please call us back with any further questions or concerns.

Future Directions for OPAL

- OPAL-G
- E-Consults
- Telepsychiatry
- Your ideas

OPAL-G

- Partnership with OHA's Older Adult Behavioral Health Services
- Focused on older adults in long term residential care
- Pilot site selected

E-Consults

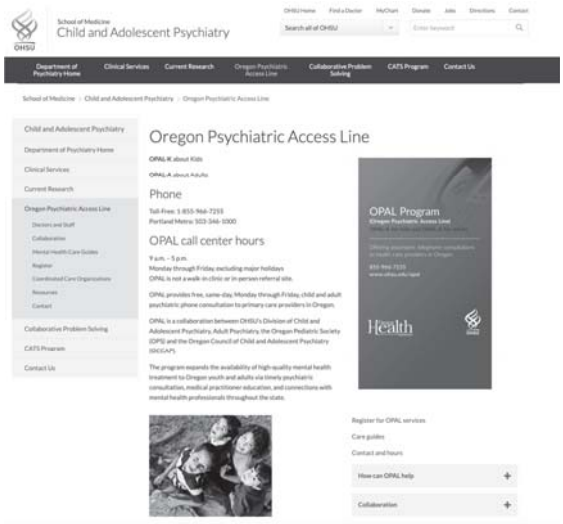
- Consults completed by secure email
- Requires HIPAA-compliant framework accessible to any LMP in the state
- CMS has approved billing for eConsults

Telepsychiatry Consults

- Assessments completed by videoconferencing
- Requires HIPAA-compliant framework accessible by any clinic in the state
- Billable to most insurance companies

Your Ideas?

- OPAL grew out of a desire to fill unmet needs
- OPAL's nature has already generated several adaptations
- In what ways can OPAL continue to evolve to best meet the needs of Oregon?



Thank You

In-Flight Medical Events

Riana Wurzburger, MD, MPH

February 05, 2020

Video summary of article. https://www.nejm.org/do/10.1056/NEJMdo005001/full/ . Accessed June 20, 2019.

Disclosure Information

PPMC Medical Grand Rounds
February 5, 2020
Riana Wurzburger

I have no financial relationships to disclose

Sample Case

Abrahams J, Zucker D, Zucker J. *Airplane!* [Video]. Paramount Pictures;1980. YouTube. https://www.youtube.com/watch?v=OFFYIECEPag. Published May 31, 2016, Accessed February 5, 2020.

Flight Plan

- Epidemiology
- The Medical Events
- Medico-legal Issues
- Available Resources
- An Approach
- Landing Points

Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.

Zurich School of Applied Sciences. *A Day in the Life of Air Traffic Over the World*. YouTube. https://www.youtube.com/watch?v=G1L4GUABaiY. Feb 20. 2010. Accessed February 3, 2020.

International Air Transport Association. Traveler Numbers Reach New Heights. Press Release No. 51, Sept 6, 2018. Accessed June 20, 2019. https://www.iata.org/pressroom/pr/Pages/2018-09-06-01.aspx

Definitions

In-Flight Medical Event

- Any medical event that occurs in-flight

In-Flight Medical Emergency

- A medical event that requires:
  - Medical supplies other than those intended for first aid
  - A doctor's advice from ground medical support
  - The help of an onboard volunteer
  - Or that results in diversion or death

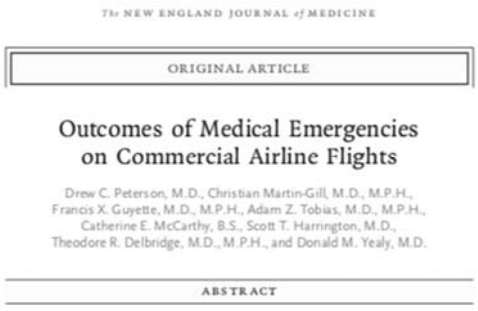
Aerospace Medical Association Air Transport Medicine Committee. Medical Emergencies: Managing In-Flight Medical Events. July 2016. http://www.asma.org/asma/media/AsMA/Travel-Publications/Medical%20Guidelines/In-flight-medical-events-guidance-document-revised-July-2016.pdf.

How Often Do In-Flight Medical Emergencies Occur?

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Epstein CR, Forbes JM, Futter CL et al. Frequency and clinical spectrum of in-flight medical incidents during domestic and international flights. *Anaesthesia and Intensive Care.* Feb 13, 2019. doi 10.1177/0310057X18811748

How Often Do In-Flight Medical Emergencies Occur?



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Outcomes of Medical Emergencies on Commercial Airline Flights

Drew C. Peterson, M.D., Christian Martin-Gill, M.D., M.P.H., Francis X. Guyette, M.D., M.P.H., Adam Z. Tobias, M.D., M.P.H., Catherine E. McCarthy, B.S., Scott T. Harrington, M.D., Theodore R. Delbridge, M.D., M.P.H., and Donald M. Yealy, M.D.

ABSTRACT

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Epstein CR, Forbes JM, Futter CL et al. Frequency and clinical spectrum of in-flight medical incidents during domestic and international flights. *Anaesthesia and Intensive Care.* Feb 13, 2019. doi 10.1177/0310057X18811748

How Often Do In-Flight Medical Emergencies Occur?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Outcom rgencies on Co lights

Drew C. Pete M.D., M.P.H., Francis X. Guyett M.D., M.P.H., Catherine E. McCarthy, B.S., Scott T. Harrington, M.D., Theodore R. Delbridge, M.D., M.P.H., and Donald M. Yealy, M.D.

ABSTRACT

1 in 604 flights

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Epstein CR, Forbes JM, Futter CL et al. Frequency and clinical spectrum of in-flight medical incidents during domestic and international flights. *Anaesthesia and Intensive Care.* Feb 13, 2019. doi 10.1177/0310057X18811748

How Often Do In-Flight Medical Emergencies Occur?

Anaesthesia and Intensive Care

View all publication partners

1.358

Home Browse Submit Paper About Subscribe

Search: keywords, title, autho

Article Menu Close

Download PDF

Full Article

Frequency and clinical spectrum of in-flight medical incidents during domestic and international flights

Catherine R Epstein, James M Forbes, Christopher L Futter, more...

Show all auth

First Published February 13, 2019 | Research Article

https://doi.org/10.1177/0310057X18811748

Article information

Altmetric 4

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Epstein CR, Forbes JM, Futter CL et al. Frequency and clinical spectrum of in-flight medical incidents during domestic and international flights. *Anaesthesia and Intensive Care.* Feb 13, 2019. doi 10.1177/0310057X18811748

How Often Do In-Flight Medical Emergencies Occur?

Anaesthesia and Intensive Care

View all publication partners

1.358

Home Browse Submit P

Search: keywords, title, autho

Article Menu Close

Download PDF

Full Article

incidents during domestic and

Show all auth

First Published February 13, 2019 | Research Article

https://doi.org/10.1177/0310057X18811748

Article information

Altmetric 4

1 in 150 flights

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Epstein CR, Forbes JM, Futter CL et al. Frequency and clinical spectrum of in-flight medical incidents during domestic and international flights. *Anaesthesia and Intensive Care.* Feb 13, 2019. doi 10.1177/0310057X18811748

- **1 medical emergency in every 604 flights**
- 44,000 in-flight emergencies annually
- Occurs daily
- Likely an underestimate

ORIGINAL ARTICLE

Outcomes of Medical Emergencies on Commercial Airline Flights

Drew C. Peterson, M.D., Christian Martin-Gill, M.D., M.P.H., Francis X. Guyette, M.D., M.P.H., Adam Z. Tobias, M.D., M.P.H., Catherine E. McCarthy, B.S., Scott T. Harrington, M.D., Theodore R. Delbridge, M.D., M.P.H., and Donald M. Yealy, M.D.

ABSTRACT

BACKGROUND

Worldwide, 2.75 billion passengers fly on commercial airlines annually. When in-flight medical emergencies occur, access to care is limited. We describe in-flight medical emergencies and the outcomes of these events.

METHODS

We reviewed records of in-flight medical emergency calls from five domestic and international airlines to a physician-directed medical communications center from January 1, 2008, through October 31, 2010. We characterized the most common medical problems and the type of on-board assistance rendered. We determined the incidence of and factors associated with unscheduled aircraft diversion, transport to a hospital, and hospital admission, and we determined the incidence of death.

RESULTS

There were 11,920 in-flight medical emergencies resulting in calls to the center (1 medical emergency per 604 flights). The most common problems were syncope or presyncope (37.4% of cases), respiratory symptoms (12.3%), and nausea or vomiting (9.5%). Physician passengers provided medical assistance in 48.2% of in-flight medical emergencies, and aircraft diversion occurred in 7.3%. Of 10,924 patients for whom postflight follow-up data were available, 25.8% were transported to a hospital by emergency-medical-service personnel, 8.6% were admitted, and 0.3% died. The most common triggers for admission were possible stroke (odds ratio, 3.36; 95% confidence interval [CI], 1.88 to 6.01), respiratory symptoms (odds ratio, 2.13; 95% CI, 1.48 to 3.06), and cardiac symptoms (odds ratio, 1.95; 95% CI, 1.37 to 2.77).

CONCLUSIONS

Most in-flight medical emergencies were related to syncope, respiratory symptoms, or gastrointestinal symptoms, and a physician was frequently the responding medical volunteer. Few in-flight medical emergencies resulted in diversion of aircraft or death; one fourth of passengers who had an in-flight medical emergency underwent additional evaluation in a hospital. (Funded by the National Institutes of Health.)

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Why an Underestimate?

System-wide global commercial airlines	2013	2014	2015	2016	2017	2018	2019F
REVENUES, $ billion	720	767	721	709	755	812	865
% change	2.1	6.5	-6.1	-1.6	6.5	7.6	6.5
Passenger, $ billion	537	538	509	498	534	561	589
Cargo, $ billion	92.1	92.9	83.8	80.8	95.9	111.3	111.3
Traffic volumes							
Passenger growth, rpk, %	5.7	6.0	7.4	7.4	8.1	7.4	5.0
Sched passenger numbers, millions	3,145	3,328	3,569	3,817	4,095	4,378	4,579

International Air Transport Association. IATA Industry Statistics. Fact Sheet. June 2019. Accessed June 20, 2019. https://www.iata.org/pressroom/facts_figures/fact_sheets/Documents/fact-sheet-industry-facts.pdf

Flight Plan

- Epidemiology
- **The Medical Events**
- Medico-legal Issues
- Available resources
- An Approach
- Landing Points

Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.

Why Does This Happen? The In-Flight Environment

- Cabin pressure
- Humidity
- Boyle's law
- Immobility
- Stress

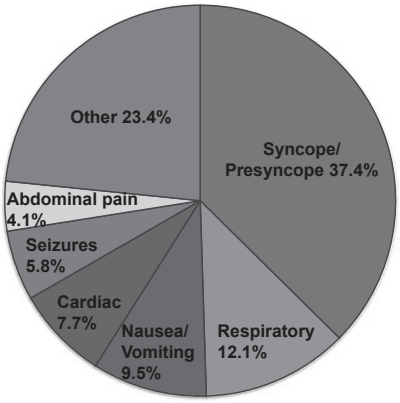
$$P_1V_1 = P_2V_2$$

P = Pressure of the gas
V = Volume of the gas

1)Donner HJ. Is There a Doctor Onboard? Medical Emergencies at 40,000 Feet . Emerg Med Clin N Am 35 (2017) 443–463. http://dx.doi.org/10.1016/j.emc.2017.01.005

Silverman D, Gendreau M. Medical issues associated with commercial flights. Lancet. 2009;373(9680):2067-77.

What Medical Events Occur?[2]



Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med*. 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Table 1. **In-Flight Medical Emergencies According to Medical-Problem Category and Outcome.**

Category	All Emergencies	Aircraft Diversion	Transport to a Hospital*	Hospital Admission†	Death
		no./total no. (%)			no.
All categories	11,920/11,920 (100)	875/11,920 (7.3)	2804/10,877 (25.8)	901/10,482 (8.6)	36
Syncope or presyncope	4463/11,920 (37.4)	221/4463 (5.0)	938/4252 (22.1)	267/4123 (6.5)	4
Respiratory symptoms	1447/11,920 (12.1)	81/1447 (5.6)	311/1371 (22.7)	141/1336 (10.6)	1
Infectious disease		**330/11,920 (2.8%)**			
Agitation/Psychiatric		**287/11,920 (2.4%)**			
Allergic reaction		**265/11,920 (2.2%)**			
Possible stroke		**238/11,920 (2.0%)**			
Trauma		**215/11,920 (1.8%)**			
Diabetic complication		**193/11,920 (1.6%)**			
symptoms					
Ear pain	49/11,920 (0.4)	1/49 (2.0)	2/43 (4.7)	1/43 (2.3)	0
Cardiac arrest	38/11,920 (0.3)	22/38 (57.9)	14/34 (41.2)	1/6 (16.7)	31
Laceration	33/11,920 (0.3)	1/33 (3.0)	3/26 (11.5)	0/25	0
Other	821/11,920 (6.9)	62/821 (7.6)	162/705 (23.0)	36/679 (5.3)	0
Unknown	8/11,920 (0.1)	0/8	0/8		0

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med*. 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Table 1. **In-Flight Medical Emergencies According to Medical-Problem Category and Outcome.**

Category	All Emergencies	Aircraft Diversion	Transport to a Hospital*	Hospital Admission†	Death
		no./total no. (%)			no.
All categories	11,920/11,920 (100)	875/11,920 (7.3)	2804/10,877 (25.8)	901/10,482 (8.6)	36
Syncope or presyncope	4463/11,920 (37.4)	221/4463 (5.0)	938/4252 (22.1)	267/4123 (6.5)	4
Respiratory symptoms	1447/11,920 (12.1)	81/1447 (5.6)	311/1371 (22.7)	141/1336 (10.6)	1
Nausea or vomiting	1137/11,920 (9.5)	56/1137 (4.9)	243/1025 (23.7)	61/994 (6.1)	0
Cardiac symptoms	920/11,920 (7.7)	169/920 (18.4)	370/813 (45.5)	162/770 (21.0)	0
Seizures	689/11,920 (5.8)	83/689 (12.0)	224/626 (35.8)	75/602 (12.5)	0
Abdominal pain	488/11,920 (4.1)	50/488 (10.2)	164/412 (39.8)	41/391 (10.5)	0
Infectious disease	330/11,920 (2.8)	6/330 (1.8)	45/239 (18.8)	8/232 (3.4)	0
Agitation or psychiatric symptoms	287/11,920 (2.4)	16/287 (5.6)	38/249 (15.3)	17/244 (7.0)	0
Allergic reaction	265/11,920 (2.2)	12/265 (4.5)	40/233 (17.2)	8/229 (3.5)	0
Possible stroke	238/11,920 (2.0)	39/238 (16.4)	92/214 (43.0)	46/196 (23.5)	0
Trauma, not otherwise specified	216/11,920 (1.8)	14/216 (6.5)	34/185 (18.4)	5/180 (2.8)	0
Diabetic complication	193/11,920 (1.6)	15/193 (7.8)	45/181 (24.9)	13/172 (7.6)	0
Headache	123/11,920 (1.0)	10/123 (8.1)	23/108 (21.3)	4/107 (3.7)	0
Obstetrical/gynecologic symptoms		**61/11,920 (0.5%)**			
Cardiac arrest		**38/11,920 (0.3%)**			
Unknown	8/11,920 (0.1)	0/8	0/8		0

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med*. 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Who is Responding?

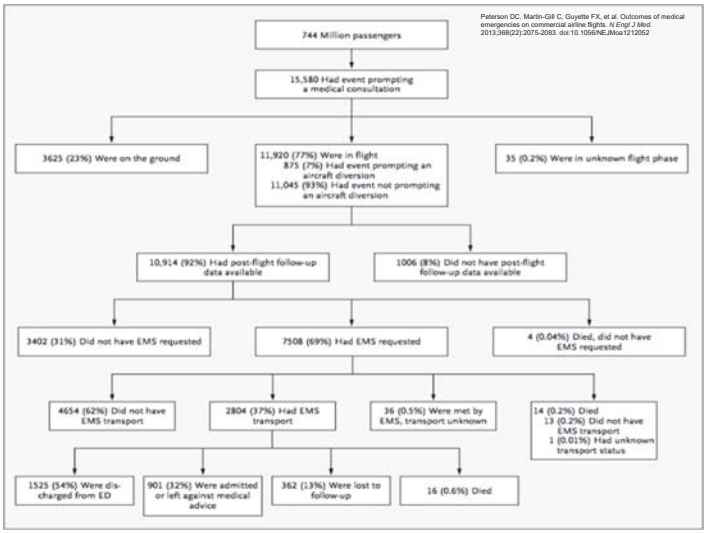
Video summary of article. https://www.nejm.org/doi/10.1056/NEJMoa1205001/full/ Accessed June 20, 2019.

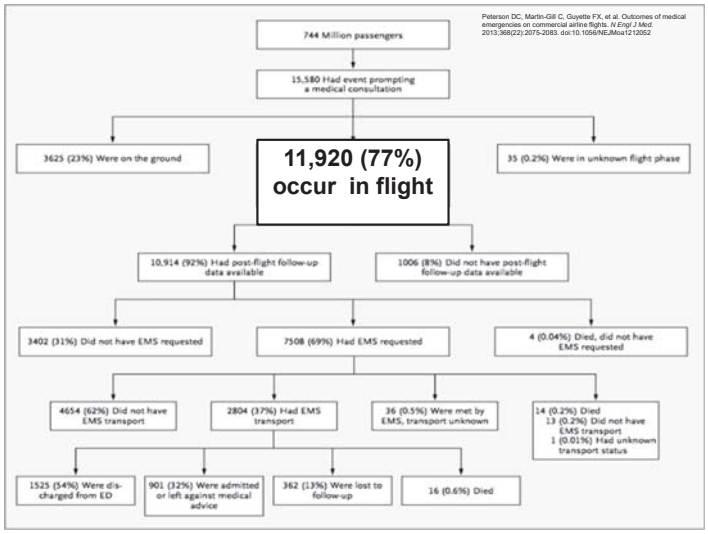
- Physicians 48.1%
- Nurses 20.1%
- EMS providers 4.4%
- Other health care professionals 3.7%
- Flight crew 23.7%

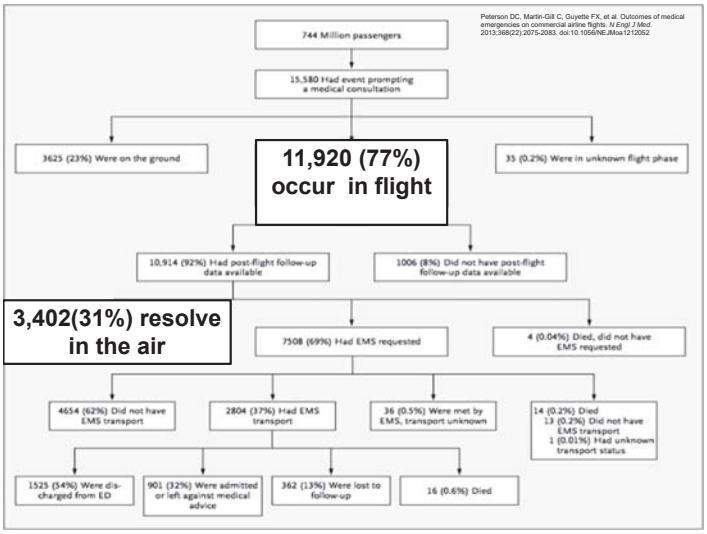
Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

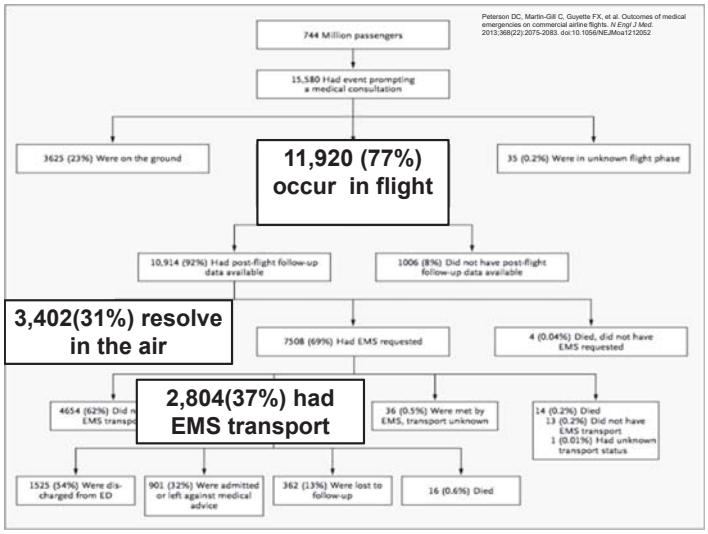
Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

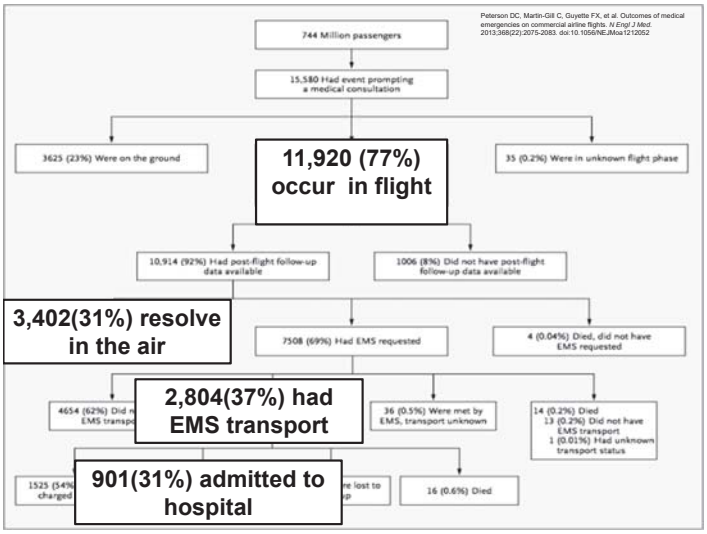
What Are The Outcomes?











Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Let's Break Down Those Numbers

Video summary of article. https://www.nejm.org/doi/10.1056/NEJMdo005981/full/ . Accessed June 20, 2019.

- 31% of cases resolve in the air
- 8.6% of cases require hospital admission
- 7% require aircraft diversion
- Mortality rate 0.3%

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med.* 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Flight Plan

- Epidemiology
- The Medical Events
- **Medico-legal Issues**
- Available Resources
- An Approach
- Landing Points

Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.

What Do I Have to Do? (Duty to Act)

[illegible] Sick Passengers Spooked on Planes. https://www.flying[illegible].com/s/weird-behavior-on-planes-5d2c1a1[illegible]5447d7. Accessed Feb 03, 2020.

- US healthcare providers are not legally required to respond on US-based airlines
- Most argue there is an ethical obligation

Nable JV, Tupe CL, Gehle BD, Brady JW. Is there a doctor on board? In-flight medical emergencies. Cleveland clinic journal of medicine. June 2017; 84(6); 457-462.

But What If…

- I've been drinking
  - Use your judgment
  - Most say don't volunteer
- I'm not that kind of doctor
  - Act within your scope
  - You're still the most knowledgeable

Flying to [illegible] Cherry Bakes. https://www.[illegible].com/[illegible]. Accessed Jun[illegible]

Wong, M. Doctor in the sky: Medico-legal issues during in-flight emergencies. Medical Law International. 2017; 17(1-2) 65–98

Can I get Sued?

1998 Aviation Medical Assistance Act (AMAA)

*An individual **shall not be held liable** for damages in any action brought in a Federal or State court arising out of the acts or omissions of the individual **in providing or attempting to provide assistance in the case of an in-flight medical emergency** unless the individual, while rendering such assistance, is guilty of **gross negligence or willful misconduct**.*

H. Rept. 105-456 - AVIATION MEDICAL ASSISTANCE ACT OF 1998
https://www.govinfo.gov/content/pkg/CRPT-105hrpt456/pdf/CRPT-105hrpt456.pdf

Can I get Sued?

There has only been one self-reported case of a doctor in the US being sued for assisting in a mid-flight emergency. The lawsuit was dismissed without hearing

Wong, M. Doctor in the sky: Medico-legal issues during in-flight emergencies. Medical Law International. 2017; 17(1-2) 65–98

Flight Plan

- Epidemiology
- The Medical Events
- Medico-legal Issues
- **Available Resources**
- An Approach
- Landing Points

Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.

What *People* are Available?

Video summary of article. https://www.nejm.org/do/10.1056/NEJMdo005001/full/ . Accessed June 20, 2019.

- Flight attendants
- Other providers on the plane
- Ground-based medical consultation
- The captain decides on diversion

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med*. 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

What *Supplies* Are Available?

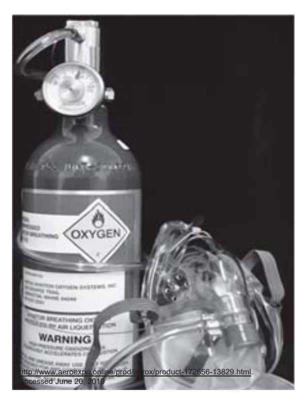
- The FAA mandates:
  - Emergency Medical Kit
  - AED
  - Oxygen
  - Basic first aid kit
- Some airlines have supplemental supplies

Donner HJ. Emerg Med Clin N Am 35 (2017) 443–463. http://dx.doi.org/10.1016/j.emc.2017.01.005

Nable JV, Tupe CL, Gehle BD, Brady JW. Is there a doctor on board? In-flight medical emergencies. Cleveland clinic journal of medicine. June 2017; 84(6); 457-462.

A Word About Oxygen

- Aircraft portable oxygen bottles have two settings
  - Low: 2 L/min
  - High: 4 L/min



http://www.aeroexpo.online/prod/aerox/product-172656-13829.html. Accessed June 20, 2019

Donner HJ. Emerg Med Clin N Am 35 (2017) 443–463. http://dx.doi.org/10.1016/j.emc.2017.01.005

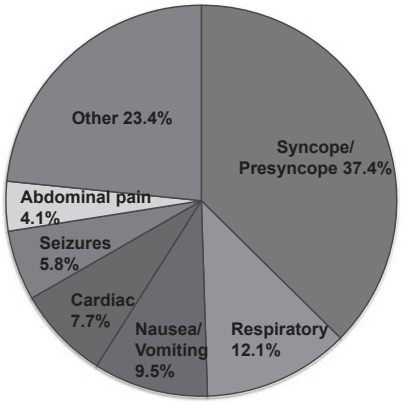
FAA Mandated Equipment	
Sphygmomanometer	Manual cuff
Stethoscope	Disposable
Oropharyngeal airway (3 sizes)	
Self-inflating manual resuscitation device with 3 masks	
CPR masks (3 sizes)	
Intravenous administration set (tubing with Y connectors)	
Needles and syringes	
Alcohol sponges	
Adhesive Tape, 1 inch	
Tape scissors	
Tourniquet (for IV placement)	
Protective gloves	
Instructions on kit use	

Emergency Medical Equipment. Advisory Circular. Federal Aviation Administration. Jan 12 2016. https://www.faa.gov/documentlibrary/media/advisory_circular/ac121-33b.pdf. Accessed June 20, 2019.

FAA Mandated Medications	
Saline solution, 500 cc	
Analgesic, non-narcotic, tablets, 325 mg	
Antihistamine tablets, 25 mg	**Allergy**
Antihistamine injectable, 50 mg	**Allergy**
Atropine, 0.5 mg, 5 cc	**Allergy**
Aspirin tablets, 325 mg	**ACS**
Bronchodilator, inhaled (metered dose inhaler)	**ACS**
Dextrose, 50%/50cc injectable	
Epinephrine 1:1000, 1 cc, injectable	**ACLS**
Epinephrine 1:10,000, 2 cc, injectable	**ACLS**
Lidocaine, 5 cc, 20 mg/ml, injectable	**ACLS**
Nitroglycerine tablets, 0.4 mg	**ACLS**
Instructions on use of drugs in the kit	

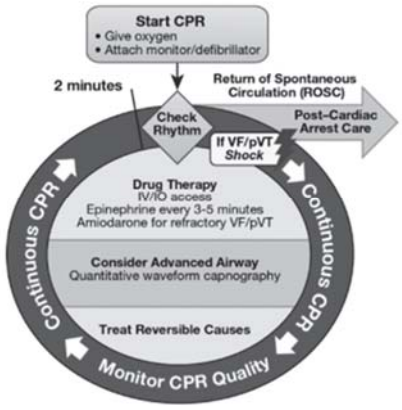
Emergency Medical Equipment. Advisory Circular. Federal Aviation Administration. Jan 12 2016. https://www.faa.gov/documentlibrary/media/advisory_circular/ac121-33b.p
Accessed June 20, 2019.

What's Missing?



Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med*. 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

What's Missing? Cardiac Arrest



ACLS Digital Reference Card Set. https://shopcpr.heart.org/acls-digital-reference-card-set. Accessed Feb 03 2020.

What's Missing?

Medical Event	Frequency	Supplies
Respiratory	12%	Pulse Oximeter
Nausea/Vomiting	9.5%	Anti-emetics
Seizure	5.8%	Benzodiazepines, Anti-epileptics
Infectious Disease	2.8%	Thermometer, Antibiotics
Agitation	2.4%	Antipsychotics
Diabetic Complications	1.6%	Glucometer
Pain	1.8%	Analgesics, Naloxone

Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med*. 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052

Flight Plan

- Epidemiology
- The Medical Events
- Medico-legal Issues
- Available resources
- **An Approach**
- Landing Points

Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.

Case

You are sitting in your s ie and eating your airplane me ear a cry for help from the bac wed by for assistance from any me nboard.* You approach the are flight attendants are talking wit senger and what appears to be another volunteer.*

1. Determine if you can and will respond

2. Identify yourself and state your credentials

Case

An older woman is slumped in unconscious. She is accompa husband, who appears very nervous. Y yourself and ask permission to help*. You ask the flight attendant for access to the EMK*.

3. Ask permission if able

4. Ask the crew for the EMK

Case

5. Obtain vitals early

6. Perform a targeted exam

*VS: RR 14, pulse ~100, regular

Exam: diaphoretic, does not wake to voice or sternal rub*

History: her husband says that she complained of feeling nauseated, stood up to use the la passed out into her seat. No known card no complaints of chest pain or shortness of preceding. She had two glasses of wine on the plane.*

7. Take a focused history

Case

The crew returns with the EMK

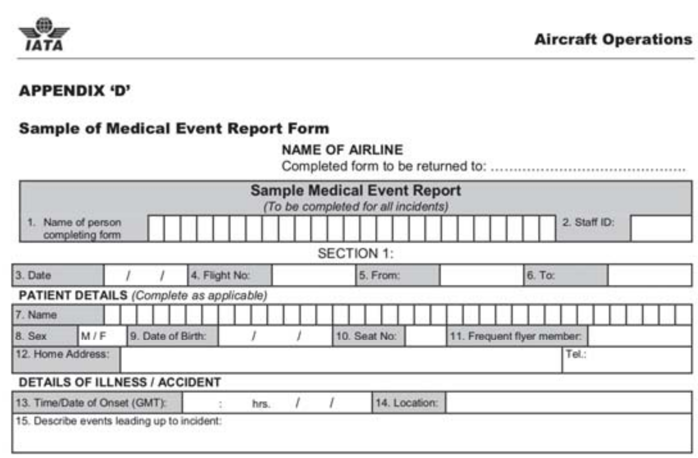
Manual BP is 90/60

Suspecting syncope, you ask the crew to help lower the woman to the g orm a leg raise.* The woman wakes e feels fain localizing comp er remai water, and after 30 minutes, a repeat BP feels better and you both return to your seats.* You record the events on an airline-provided form.*

8. Provide treatment. Act within your scope

9. Stay until resolution or transfer of care

10. Document the encounter



IATA — Aircraft Operations

APPENDIX 'D'

Sample of Medical Event Report Form

NAME OF AIRLINE
Completed form to be returned to: ....

Sample Medical Event Report
(To be completed for all incidents)

1. Name of person completing form | 2. Staff ID:

SECTION 1:

3. Date / / | 4. Flight No: | 5. From: | 6. To:

PATIENT DETAILS (Complete as applicable)

7. Name

8. Sex M / F | 9. Date of Birth: / / | 10. Seat No: | 11. Frequent flyer member:

12. Home Address: | Tel.:

DETAILS OF ILLNESS / ACCIDENT

13. Time/Date of Onset (GMT): : hrs. / / | 14. Location:

15. Describe events leading up to incident:

International Medical Manual 11th Edition. 2018 International Air Transport Association. Montreal Geneva. https://www.iata.org/contentassets/66e68bc255da4b2eaf0cbfe3657e9332/medical-manual.pdf Access Feb 03 2020

General Tips

- Keep a calm demeanor
- Keep crew informed
- You can ask for help
- You can recommend diversion
- Remember the captain has the ultimate say

Abrahams J, Zucker D, Zucker J. *Airplane!* [Video]. Paramount Pictures;1980. YouTube. https://www.youtube.com/watch?v=DFPYECEPaq. Published May 31, 2016. Accessed February 5, 2020.

When To Suggest Diversion

- Unremitting chest pain
- Severe shortness of breath
- Severe abdominal pain
- Suspected stroke
- Persistent unresponsiveness
- Refractory seizures
- Severe agitation

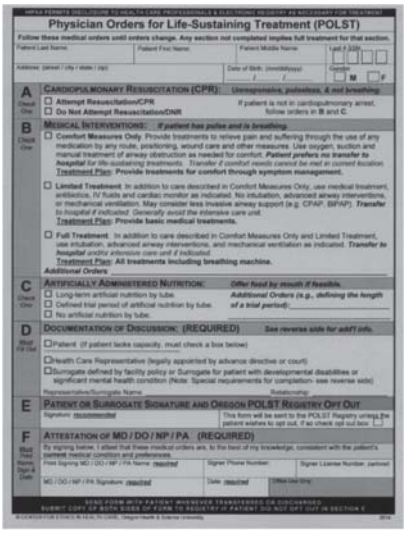
Silverman D, Gendreau M. Medical issues associated with commercial flights. Lancet. 2009;373(9680):2067-77.

Cardiac Arrest or Death

IATA

Death on board

International Air Transport Association. Death on Board. Issued Jan 2018. https://www.iata.org/contentassets/ccbdc54681c24574bebf2db2b18197a5/death-on-board-guidelines.pdf



Physician Orders for Life-Sustaining Treatment (POLST)

Follow these medical orders until orders change. Any section not completed implies full treatment for that section.

Patient Last Name | Patient First Name | Patient Middle Name | Last 4 SSN

Address (street / city / state / zip) | Date of Birth (mm/dd/yyyy) | Gender: M F

A Check One — CARDIOPULMONARY RESUSCITATION (CPR): Unresponsive, pulseless, & not breathing
- Attempt Resuscitation/CPR
- Do Not Attempt Resuscitation/DNR

If patient is not in cardiopulmonary arrest, follow orders in B and C.

B Check One — MEDICAL INTERVENTIONS: *If patient has pulse and is breathing*
- Comfort Measures Only. Provide treatments to relieve pain and suffering through the use of any medication by any route, positioning, wound care and other measures. Use oxygen, suction and manual treatment of airway obstruction as needed for comfort. *Patient prefers no transfer to hospital for life-sustaining treatments. Transfer if comfort needs cannot be met in current location.* Treatment Plan: Provide treatments for comfort through symptom management.
- Limited Treatment. In addition to care described in Comfort Measures Only, use medical treatment, antibiotics, IV fluids and cardiac monitor as indicated. No intubation, advanced airway interventions, or mechanical ventilation. May consider less invasive airway support (e.g. CPAP, BiPAP). *Transfer to hospital if indicated. Generally avoid the intensive care unit.* Treatment Plan: Provide basic medical treatments.
- Full Treatment. In addition to care described in Comfort Measures Only and Limited Treatment, use intubation, advanced airway interventions, and mechanical ventilation as indicated. *Transfer to hospital and/or intensive care unit if indicated.* Treatment Plan: All treatments including breathing machine.

Additional Orders

C Check One — ARTIFICIALLY ADMINISTERED NUTRITION: *Offer food by mouth if feasible.*
- Long-term artificial nutrition by tube.
- Defined trial period of artificial nutrition by tube.
- No artificial nutrition by tube.

Additional Orders (e.g., defining the length of a trial period):

D May Fill Out — DOCUMENTATION OF DISCUSSION: (REQUIRED) *See reverse side for adult info.*
- Patient (if patient lacks capacity, must check a box below)
- Health Care Representative (legally appointed by advance directive or court)
- Surrogate defined by facility policy or Surrogate for patient with developmental disabilities or significant mental health condition (Note: Special requirements for completion- see reverse side)

Representative/Surrogate Name | Relationship

E — PATIENT OR SURROGATE SIGNATURE AND OREGON POLST REGISTRY OPT OUT

Signature: recommended | This form will be sent to the POLST Registry unless the patient wishes to opt out. If so check opt out box [ ]

F — ATTESTATION OF MD / DO / NP / PA: (REQUIRED)

By signing below, I attest that these medical orders are, to the best of my knowledge, consistent with the patient's current medical condition and preferences.

Print Signing MD / DO / NP / PA Name: required | Signer Phone Number: | Signer License Number: (advised)

MD / DO / NP / PA Signature: required | Date: required | Office Use Only

SEND FORM WITH PATIENT WHENEVER TRANSFERRED OR DISCHARGED
SUBMIT COPY OF BOTH SIDES OF FORM TO REGISTRY IF PATIENT DID NOT OPT OUT IN SECTION E

Oregon POLST. https://oregonpolst.org/polstnews/2015/1/30/2014-version-of-the-polst-form-released. Accessed Feb 03 2020.

Where To Find Guidelines

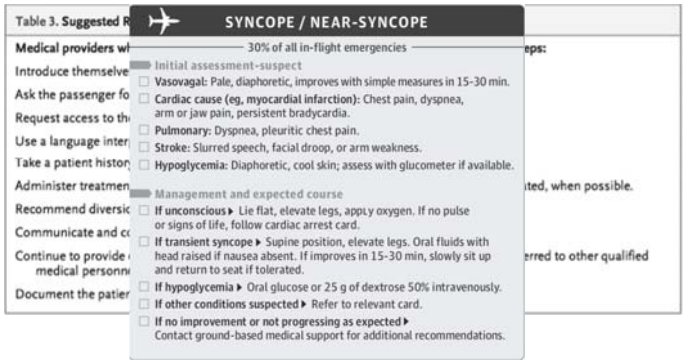


Table 3. Suggested R

Medical providers wi

Introduce themselve

Ask the passenger fo

Request access to th

Use a language inter

Take a patient histor

Administer treatmen

Recommend diversic

Communicate and cc

Continue to provide medical personn

Document the patier

eps:

ted, when possible.

erred to other qualified

SYNCOPE / NEAR-SYNCOPE

30% of all in-flight emergencies

Initial assessment-suspect

- Vasovagal: Pale, diaphoretic, improves with simple measures in 15-30 min.
- Cardiac cause (eg, myocardial infarction): Chest pain, dyspnea, arm or jaw pain, persistent bradycardia.
- Pulmonary: Dyspnea, pleuritic chest pain.
- Stroke: Slurred speech, facial droop, or arm weakness.
- Hypoglycemia: Diaphoretic, cool skin; assess with glucometer if available.

Management and expected course

- If unconscious ▸ Lie flat, elevate legs, apply oxygen. If no pulse or signs of life, follow cardiac arrest card.
- If transient syncope ▸ Supine position, elevate legs. Oral fluids with head raised if nausea absent. If improves in 15-30 min, slowly sit up and return to seat if tolerated.
- If hypoglycemia ▸ Oral glucose or 25 g of dextrose 50% intravenously.
- If other conditions suspected ▸ Refer to relevant card.
- If no improvement or not progressing as expected ▸ Contact ground-based medical support for additional recommendations.

Aerospace Medical Association Air Transport Medicine Committee. Medical Emergencies: Managing In-Flight Medical Events. July 2016. http://www.asma.org/asma/media/AMA/Travel-Publications/Medical%20Guidelines/In-flight-medical-events-guidance-document-revised-July-2016.pdf

Nable JV, Tupe CL, Gehle BD, Brady WJ. In-Flight Medical Emergencies during Commercial Travel. N Engl J Med. 2015;373(10):939-45.

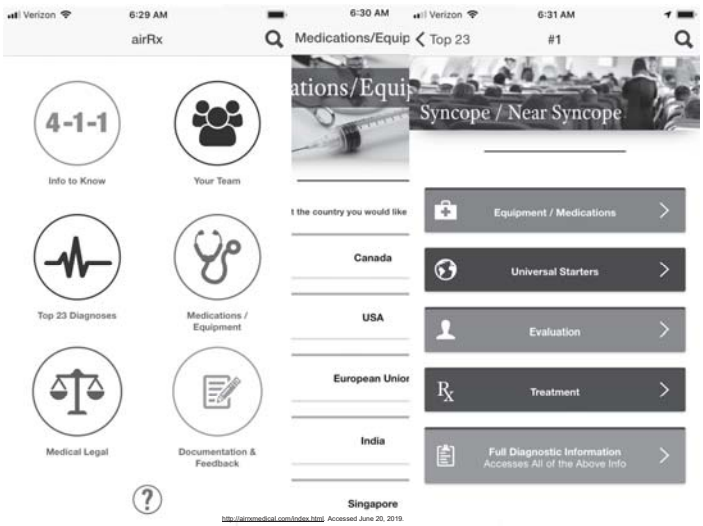
Martin-Gill C, Doyle TJ, Yealy DM. Guyette FX, et al. In-Flight Medical Emergencies. A Review. JAMA. 2018;320(24):2580-2590. doi:10.1001/jama.2018.19842

airRx

Free Download on iOS

Free Download on Android

http://airrxmedical.com/index.html. Accessed June 20, 2019.



http://airxmedical.com/index.html. Accessed June 20, 2019.

Flight Plan

- Epidemiology
- The Medical Events
- Medico-legal Issues
- Available resources
- An Approach
- **Landing Points**


Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.

Landing Points

- In-flight medical events occur regularly, but they are typically less severe than feared
- You are not legally obligated to respond, and you will have legal protection if you do
- You will have limited medical resources available
- You can consult with ground-based medical physicians

Thank You


Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.

References

1) International Air Transport Association. Traveler Numbers Reach New Heights. Press Release No. 51. Sept 6, 2018. Accessed June 20, 2019. https://www.iata.org/pressroom/pr/Pages/2018-09-06-01.aspx
2) Aerospace Medical Association Air Transport Medicine Committee. Medical Emergencies: Managing In-Flight Medical Events. July 2016. http://www.asma.org/asma/media/AsMA/Travel-Publications/Medical%20Guidelines/In-flight-medical-events-guidance-document-revised-July-2016.pdf.
3) Peterson DC, Martin-Gill C, Guyette FX, et al. Outcomes of medical emergencies on commercial airline flights. *N Engl J Med*. 2013;368(22):2075-2083. doi:10.1056/NEJMoa1212052
4) Epstein CR, Forbes JM, Futter CL et al. Frequency and clinical spectrum of in-flight medical incidents during domestic and international flights. *Anaesthesia and Intensive Care.* Feb 13, 2019. doi 10.1177/0310057X18811748
5) International Air Transport Association. IATA Industry Statistics. Fact Sheet. June 2019. Accessed June 20, 2019. https://www.iata.org/pressroom/facts_figures/fact_sheets/Documents/fact-sheet-industry-facts.pdf
6) Mahony PH, Myers JA, Larsen PD, Powell DMC, Griffiths RF. Symptom-Based Categorization of In-Flight Passenger Medical Incidents. *Aviation, Space, and Environmental Medicine*. 2011;82(12):1131-1137. doi:10.3357/asem.3099.2011
7) Kesapli M, Akyol C, Gungor F, Akyol AJ, Guven DS, Kaya G. Inflight Emergencies During Eurasian Flights. *Journal of Travel Medicine*. 2015;22(6):361-367. doi:10.1111/jtm.12230.
8) International Air Transport Association. IATA Industry Statistics. Fact Sheet. June 2019. Accessed June 20, 2019. https://www.iata.org/pressroom/facts_figures/fact_sheets/Documents/fact-sheet-industry-facts.pdf
9) Nable JV, Tupe CL, Gehle BD, Brady JW. Is there a doctor on board? In-flight medical emergencies. Cleveland clinic journal of medicine. June 2017; 84(6); 457-462.
10) Donner HJ. Is There a Doctor Onboard? Medical Emergencies at 40,000 Feet . Emerg Med Clin N Am 35 (2017) 443–463. http://dx.doi.org/10.1016/j.emc.2017.01.005
11) Emergency Medical Equipment. Advisory Circular. Federal Aviation Administration. Jan 12 2016. https://www.faa.gov/documentlibrary/media/advisory_circular/ac121-33b.pdf. Accessed June 20, 2019.
12) Martin-Gill C, Doyle TJ, Yealy DM. Guyette FX, et al. In-Flight Medical Emergencies. A Review. *JAMA.* 2018;320(24):2580-2590. doi:10.1001/jama.2018.19842
13) https://www.govinfo.gov/content/pkg/CRPT-105hrpt456/pdf/CRPT-105hrpt456.pdf
14) Wong, M. Doctor in the sky: Medico-legal issues during in-flight emergencies. Medical Law International. 2017; 17(1-2) 65–98
15) Adwani SH, Jhorar P, Grants-Kels JM. Is there a doctor onboard?: The ethical conundrum of a specialist asked to provide in-flight medical assistance. J Am Acad Dermatol 2018;79:387-9.jj-8. Bukowski JH, Richards JR. Commercial airline in-flight emergency: medical student response and review of medicolegal issues. The Journal of Emergency Medicine, Vol. 50, No. 1, pp. 74–78, 2016
16) Aviation Medical Assistance Act of 1998, Pub L. No. 105-170. Washington, DC: National Archives and Records Ad- ministration, 1998.
17) Silverman D, Gendreau M. Medical issues associated with commercial flights. Lancet. 2009;373(9680):2067-77.
18) International Medical Manual 11th Edition. 2018 International Air Transport Association. Montreal Geneva. https://www.iata.org/contentassets/66e68bc255da4b2eaf0cbfe3657e9332/medical-manual.pdf. Access Feb 03 2020
19) International Air Transport Association. Death on Board. Issued Jan 2018. https://www.iata.org/contentassets/ccbdc54681c24574bebf2db2b18197a5/death-on-board-guidelines.pdf

Images

- Video summary of article. https://www.nejm.org/do/10.1056/NEJMdo005001/full/ . Accessed June 20, 2019.
- Abrahams J, Zucker D, Zucker J. *Airplane!* [Video]. Paramount Pictures;1980. YouTube. https://www.youtube.com/watch?v=OFFYIECEPaq. Published May 31, 2016, Accessed February 5, 2020.
- Aircraft flying above the clouds 52014. https://www.freegreatpicture.com/civil-aviation/aircraft-flying-above-the-clouds-52014. Accessed June 20, 2019.
- Zurich School of Applied Sciences. *A Day in the Life of Air Traffic Over the World.* YouTube. https://www.youtube.com/watch?v=G1L4GUA8arY. Feb 20. 2010. Accessed February 3, 2020.
- Emma Charlton. What to expect on an ultra-long-haul flight. World Economic Forum. Sept 11, 2018. https://www.weforum.org/agenda/2018/09/20-hour-flights-long-haul-quantas-perth-london/. Accessed June 20, 2019.
- Christine Haughney. Flying tips for older passengers. The New York Times. Feb 8, 2012. https://www.nytimes.com/2012/02/12/travel/for-older-fliers-plan-ahead.html. Accessed June 20, 2019.
- Strange Behaviors Spotted on Planes. https://www.farandwide.com/s/weird-behavior-on-planes-3d2c1a9686b544e7. Accessed Feb 03, 2020.
- Filling up in the Hungry Skies. https://www.shermanstravel.com/advice/filling-up-in-the-hungry-skies/. Accessed Feb 03 2020.
- Donner HJ. Emerg Med Clin N Am 35 (2017) 443–463. http://dx.doi.org/10.1016/j.emc.2017.01.005
- Oxygen tank. http://www.aeroexpo.online/prod/aerox/product-172656-13829.html. Accessed June 20, 2019
- ACLS Digital Reference Card Set. https://shopcpr.heart.org/acls-digital-reference-card-set. Accessed Feb 03 2020.
- Oregon POLST. https://oregonpolst.org/polstnews/2015/1/30/2014-version-of-the-polst-form-released. Accessed Feb 03 2020.

Bites and Stings!

Thomas DeLoughery, MD MACP FAWM @bloodman
Oregon Health & Sciences University
GENERAL HEMATOLOGY

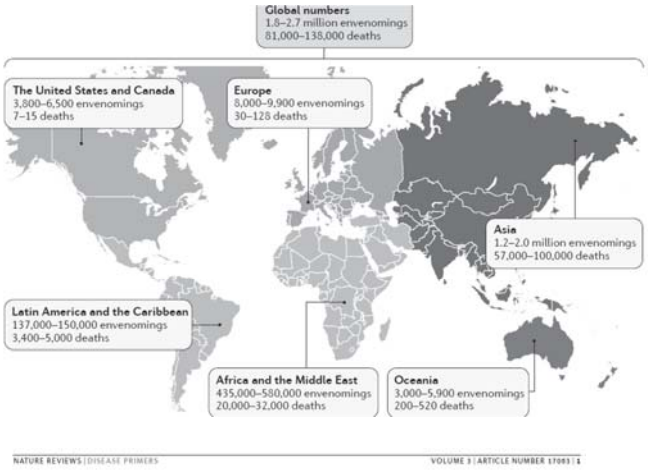
Conflicts of Interest

- None

Snake Bites

- Major issue world wide
  - > 140,000 deaths
- USA
  - 6-7,000 bites and ~2.5 deaths/yr
    - US Deaths listed on Wikipedia

Name, age, gender	Date	Species	Location, comments
Priscilla Meridith, 62, female	June 12, 2019	Timber Rattlesnake	Waverly, Georgia ; Meridith was bit by a Timber Rattlesnake in a friend's garden on May 17th when she went to sit down. She was in a medically-induced coma for several weeks until her death on June 12th. Meridith was not given antivenom due to allergies.
Oliver "Chum" Baker, 52, male	May 25, 2019	Copperhead	Winston County, Alabama. Baker was at his home near Lewis Smith Lake when he was bitten by a copperhead snake and lost consciousness within 2 minutes. CPR was performed and he was taken to a local hospital in critical condition. Baker was later airlifted to Huntsville Hospital, where he died on May 27.[9][10]
Lawrence Walters, 70, male	June 4, 2018	Rattlesnake	Spearfish, Lawrence County, South Dakota. Walters was playing golf at the Elkhorn Ridge Golf Course in Spearfish. He was looking for a ball in tall grass when he was bitten on the ankle. He was rushed back to the clubhouse in a cart where another employee performed CPR until an ambulance arrived, but was pronounced dead at Spearfish hospital.[10]
Barry Lester, 57, male	April 29, 2018	Rattlesnake	Osage County, Oklahoma. Lester was driving down a road when he spotted the rattlesnake, he tried to move it to safety but ended up being bitten on both hands. Lester collapsed shortly after and was pronounced dead.[11]



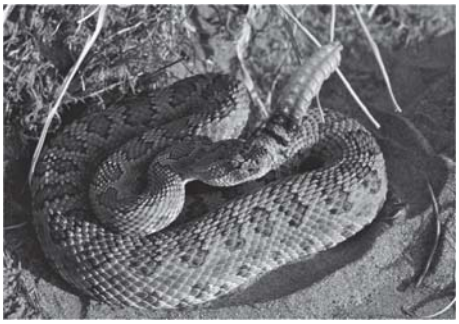
USA Venomous Snakes

- Pit Vipers
  - Rattlesnakes
  - Copperhead
  - Water moccasins
- Coral Snakes

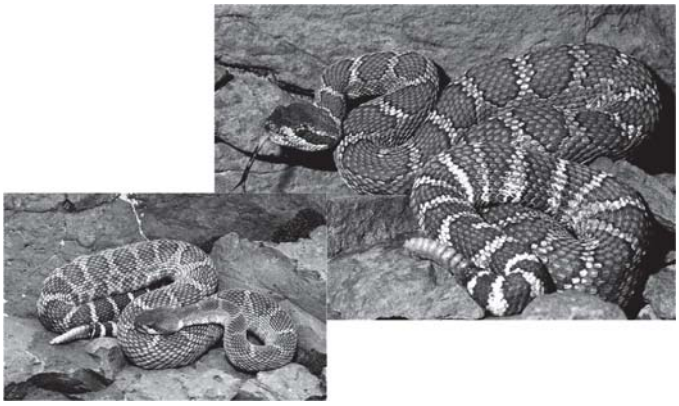
Rattlesnakes

- Has rattle!
  - New button with every skin shed
- Widespread in USA
- 4 main species with multiple subspecies
- Great Basin and Pacific in Oregon

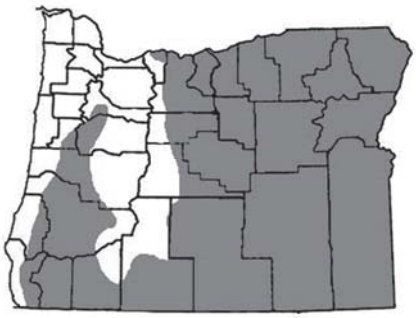
Great Basin

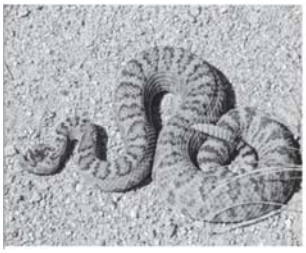


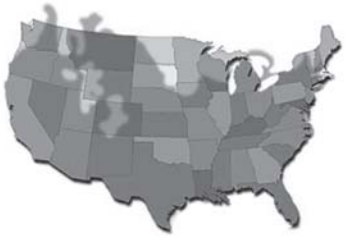
Pacific



Range in Oregon

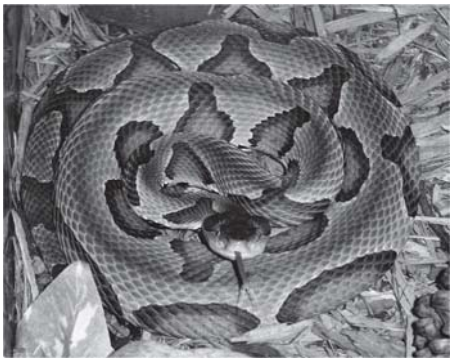






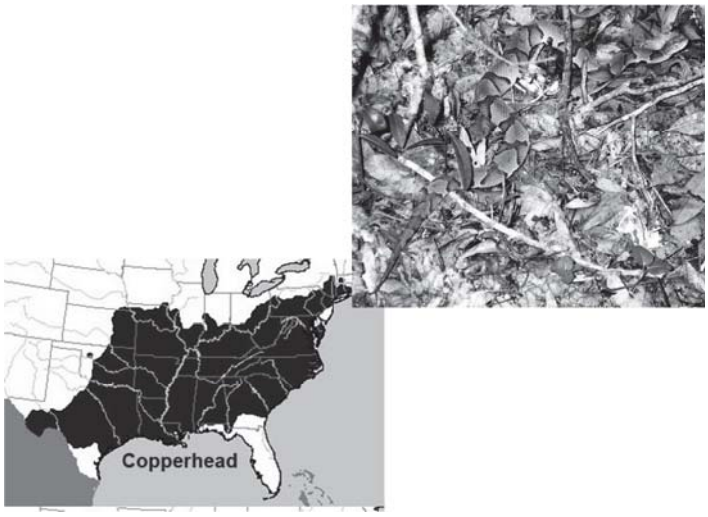
Wilderness & Environmental Medicine 2015 26, 472-487DOI: (10.1016/j.wem.2015.05.007)

Copperhead

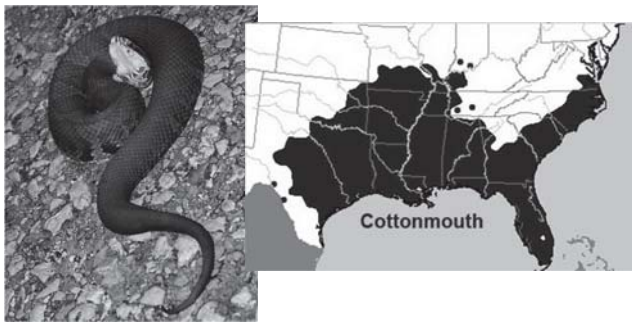


Copperhead

- Southern/Midwest US
- Hides in leaves
- Bites occur when stepped on
- Can reproduce asexually



Water Moccasin



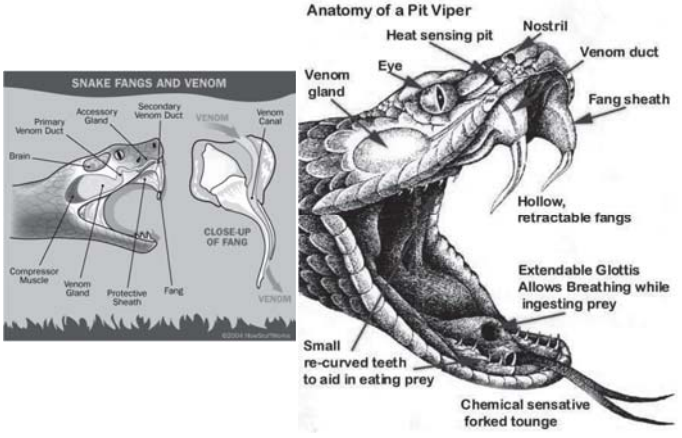
By Geoff Gallice from Gainesville

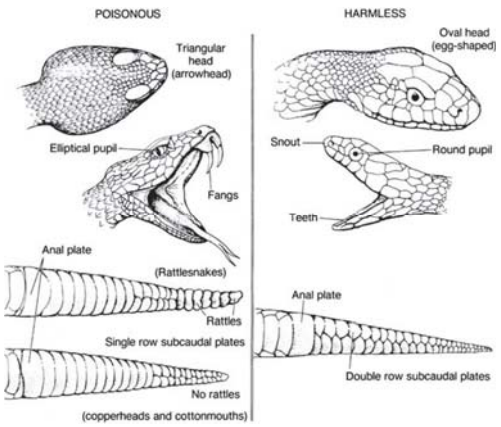
Water Moccasin

- Southern US
- Lives in/near water
- Can be aggressive
- Very muscular bodies
- Can also reproduce asexually

Pit Vipers

- Venom
- Retractable fans
- Heat sensing pit





Venom Toxicity

- Venoms composes of a bewildering array of toxins!
  - > 50 proteins
  - Local tissue damage
  - Coagulopathy
  - Neurotoxicity

Local Tissue Toxicity

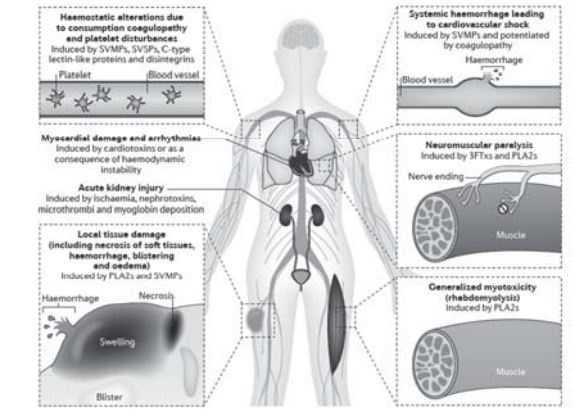
- Toxins
  - Phospholipases A2
  - Metalloproteases
  - Hyaluronidases
- Skin necrosis
- Muscle necrosis
- Disrupts vascular integrity

Neurotoxicity

- Not as dramatic as elapids
- Mojave rattlesnake exception
  - Bites tend to behave as elapid bites

Hemostasis

- Metalloproteases
- Serine proteases
- Tissue factor release
- Interference with platelets



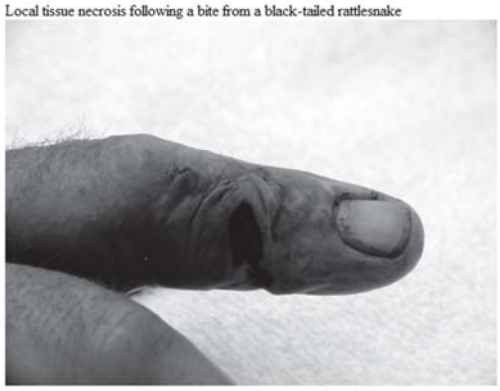
Viper Bites

- Local
  - Pain:
  - Swelling and erythema:
  - Bleeding/ecchymosis:
  - Blistering

Viper Bites

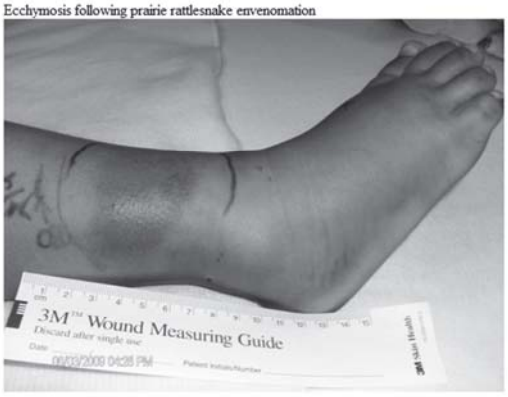
- Local evolution
  - Swelling and ecchymosis develops in an hour
  - Progression and necrosis worrisome signs
  - 25% "dry bites"

Local tissue necrosis following a bite from a black-tailed rattlesnake



This picture shows local tissue damage with necrosis after a bite to the finger by a black-tailed rattlesnake (*Crotalus molossus*). The patient was a professional herpetologist who was bitten while handling the snake.
Reproduced with permission from Daniel E. Keyler, PharmD, FAACT UpToDate®

Ecchymosis following prairie rattlesnake envenomation



Ecchymosis following prairie rattlesnake (*Crotalus viridis*) envenomation. This picture shows the extent of ecchymosis 24 hours after the bite in a 4-year-old child who was bitten while walking in a field behind a tractor.
Reproduced with permission from Daniel E. Keyler, PharmD, FAACT. UpToDate®

Viper Bites

- Systemic
  - Shock
  - Diffuse bleeding
    - Especially sites of trauma
  - Dysrhythmias

Envenomation	Observation	Laboratory Studies	Treatment
Dry/no bite	≥8 hours	Initial laboratory studies**	No antivenom
Minor: nonprogressive symptoms without systemic signs	12–24 hours	Initial laboratory studies; repeat laboratory studies†† every 4–6 hours and before discharge	Consider antivenom only if high-risk areas affected (eg, hand or face)
Moderate: progressive symptoms and/or systemic signs	Admit	Initial laboratory studies; repeat every 1 hour after antivenom until initial control	Antivenom administration, supportive care
Severe: progressive symptoms with systemic signs and/or end-organ damage	Admit	Initial laboratory studies; repeat every 1 hour after antivenom until initial control	Antivenom administration, supportive care

Wilderness & Environmental Medicine 2015 26, 472-487DOI: (10.1016/j.wem.2015.05.007)

Emergency medicine care of crotaline envenomations

Envenomation	Observation	Laboratory Studies	Treatment
Dry/no bite	≥8 hours	Initial laboratory studies*,†	No antivenom
Minor: nonprogressive symptoms without systemic signs	12–24 hours	Initial laboratory studies; repeat laboratory studies‡,† every 4–6 hours and before discharge	Consider antivenom only if high-risk areas affected (eg, hand or face)
Moderate: progressive symptoms and/or systemic signs	Admit	Initial laboratory studies; repeat every 1 hour after antivenom until initial control	Antivenom administration, supportive care
Severe: progressive symptoms with systemic signs and/or end-organ damage	Admit	Initial laboratory studies; repeat every 1 hour after antivenom until initial control	Antivenom administration, supportive care

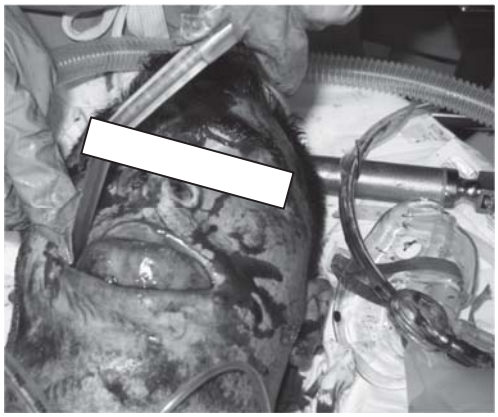
Wilderness & Environmental Medicine 2015 26, 472-487DOI: (10.1016/j.wem.2015.05.007)

Treatment

- Get bite victim to hospital ASAP
- DON'T use local therapy to remove venom
  - Cause more harm than good

Assessment

- Physical exam of wound area
  - Ecchymosis, swelling
  - Location of bite
- Labs
  - INR/PTT/Fibrinogen/Platelets
- Edema
  - Can be marked and confused for compartment syndrome



Antivenin (Vipers)

- Consult with poison center or toxicologist
- CroFab
  - Fab fragments raised to all US vipers
  - T1/2 shorter than snake venom
- Anavip
  - Fab2 fragments
    - Bigger so longer t1/2
  - Only for rattlesnakes

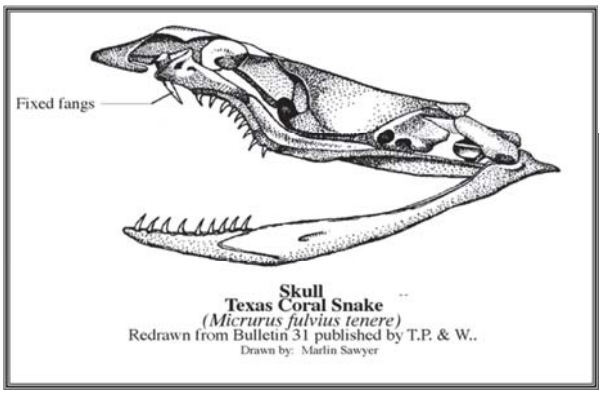
Elapids

- Bites not as dramatic
- Flaccid paralysis
  - Can progress to respiratory paralysis
- Coral snakes, cobras, death adders, mambas

Coral Snakes

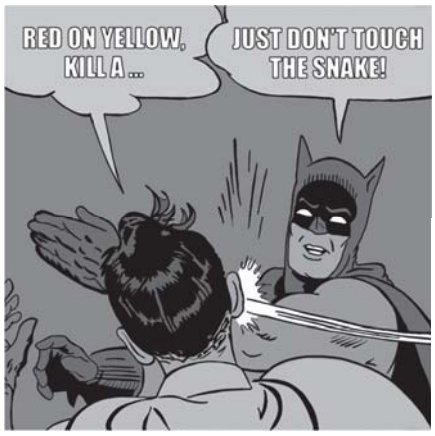
- Fixed fangs
  - Need to chew on victim

Coral Snake



Neurotoxicity

- α-neurotoxins
  - Bind cholinergic receptor->paralysis
- β-neurotoxins
  - Bind pre-synaptic and lyse nerve terminal membraned
- Very tight binding to receptors
- Leads to prolong and severe paralysis



Coral Snakes

- May need intubation
- Trial of anticholinesterase therapy
- Antivenin for severe cases
  - Limited available
  - Lots expired

Dosing

- Based on severity of bite and not patient size
- Anaphylaxis very rare

Necrotic Spider Bites

<u>Necrotic Arachnidism:</u>

- Brown Recluse Spider

(a.k.a.. fiddle-back, violin spider)

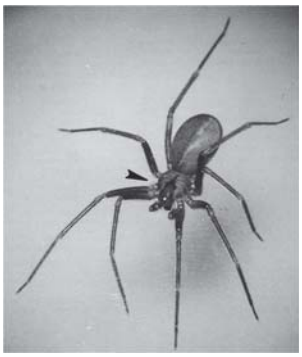
Loxosceles reclusa

Loxosceles deserta

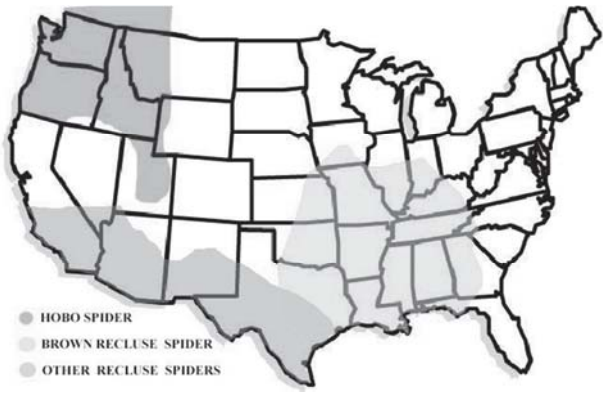
- Hobo Spider (Pacific NW)

Tegenaria agrestis

Brown Recluse Spider: violin back spider



Hobo/Brown Recluse Spider Distribution



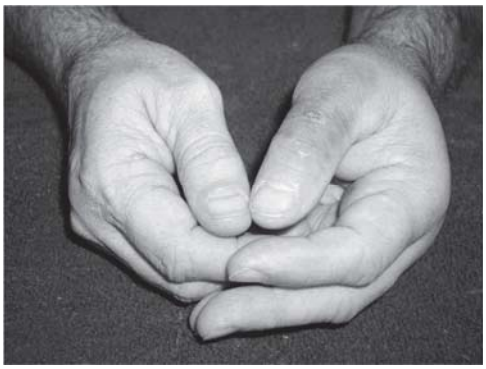
Brown Recluse

- Approx. 2000 bites/yr in US
- Begins with minor "bite" pain
- Enlarging erythema over 2 to 6 hrs
- Onset necrotic central ulcer > 24 hrs
- No ulcer by day 4 = no risk skin loss
- Nausea, vomiting, fever, arthralgia,
- Hemolytic anemia (1%)
- Delayed skin grafting (3 -5 %)

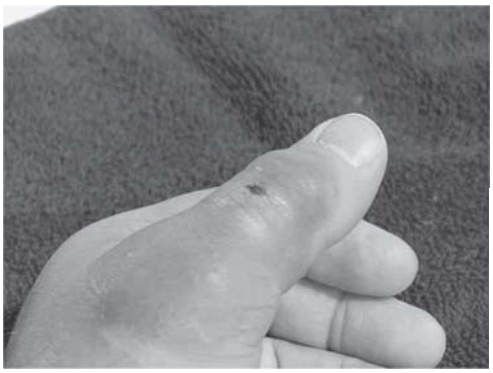
Brown Recluse

- Very potent venom
- Sphingomyelinase D
  - Dissolved cell membranes
  - Leads to a cascade of inflammatory effects
- Systemic reactions
  - Hemolysis

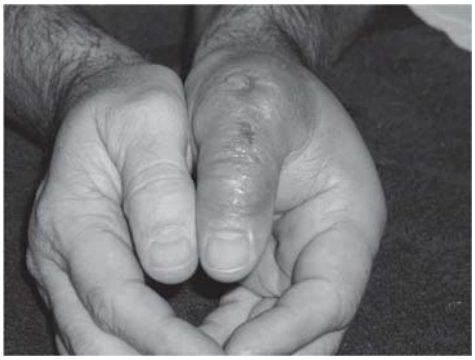
DAY 3



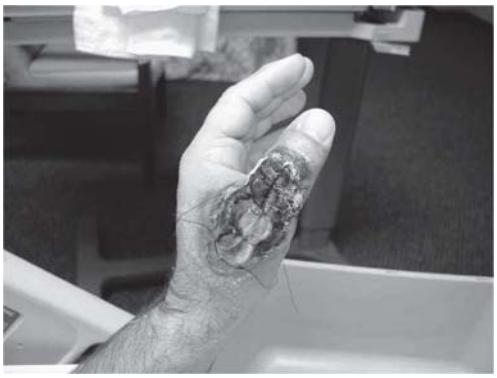
DAY 5



DAY 6



DAY 9



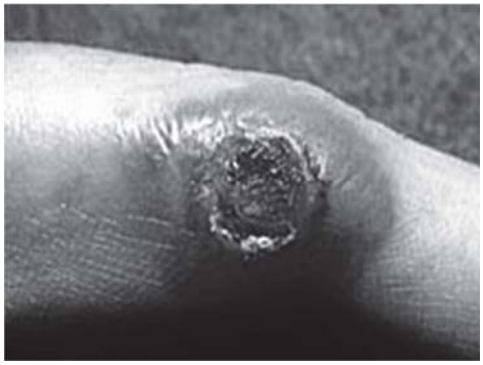
DAY 10

Hobo Spider Range

Hobo Spider

- Similar painless bite
- Headache and myalgias may occur within ½ to 1 hour and be persistent
- Blisters 1st day
- Lesion can form with central ulcer

Fig. 4 left - giant house spider
right - hobo spider
Photo by R. Vetter



Black Widow

Black Widow Spider

- Occurs in every state except Alaska
- Hourglass on underside of abdomen
- Only female has venom
- Typically outdoor near woodpiles, outhouses, sheds

Black Widow Spider

- Very painful bite
- May spread centrally over hours to days
- Diaphoresis
- Hypertension
- GI sx – esp. leg bites
- Needs parental narcotics plus benzodiazepines

Alpha-latrotoxin

- Alpha-latrotoxin: calcium mediated presynaptic neurotransmitter release
- Muscle contractions, but iv calcium probably does little to resolve it.
- Antivenin available for refractory cases but effectiveness is uncertain

Hymenoptera Stings

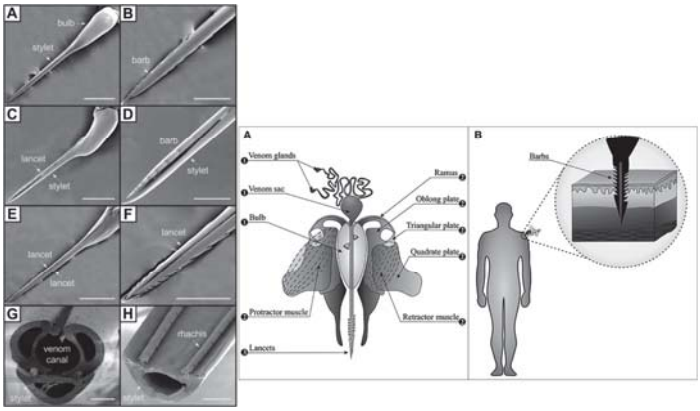
- Usually local reactions
- Multiple stings
  - Lethal dose 20 stings/kg
  - Shock/DIC/MOF
- Anaphylaxis
  - Deadly

Wasp Venom

- Rich in histamine
- Bradykinins
- Phospholipases, etc.
- Marked pain and local reactions
- 10% of patients with large local reactions

Bee Stings

- Bee's live 1-5 days after sting
- 90% venom delivered first 20 seconds
  - 150 ug venous
  - LD50 is 2.8-3.5 mg/kg
- Melittin main component
  - Act on pain fibers
  - Lytic protein
- Phospholipase A2



Anaphylaxis

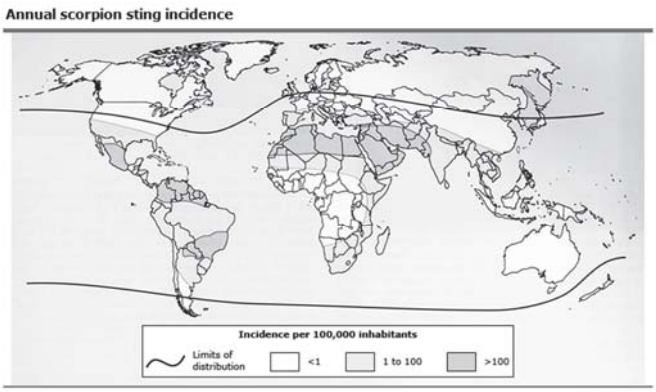
- Up to 8% population effects
  - ~ 40 deaths/yr (prob higher)
  - ½ never knew they had allergy
- Skin: urticarial, angioedema
  - Most common in kids
- Respiratory: pharynx edema and bronchoconstriction
- Cardiovascular: shock

Anaphylaxis

- Clinical history
- High tryptase
- Future risk with stings 30-60%
  - Reduced with venom immunotherapy
- Need to carry epinephrine

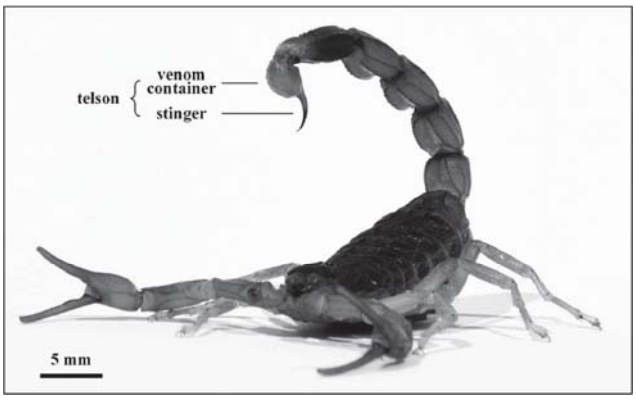
Scorpion Stings

- Found mainly in SW USA
- All scorpions sting



This figure shows the estimated annual incidence of scorpion stings by geographic region.

Reproduced from: Suchard JR. Scorpion envenomation. In: Auerbach's Wilderness Medicine, Auerbach PS (Ed), 7th ed, Elsevier, Philadelphia 2017. Illustration used with the permission of Elsevier Inc. All rights reserved.



Bark Scorpion

- Only poisonous US scorpion
- Can climb walls
- Bark scorpions have neurotoxin
  - α-toxin inhibits inactivation of sodium channels
  - No local wound effects
- Antivenin for severe cases

Symptoms

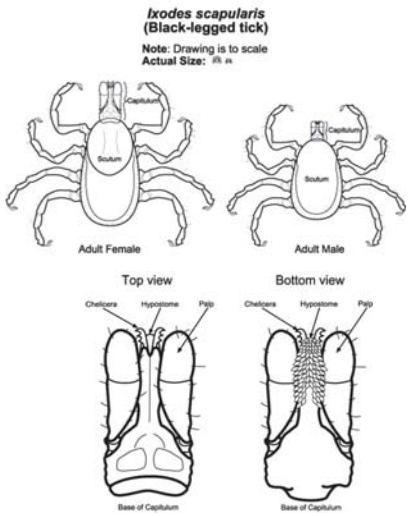
- Sting very painful
  - "tap test"
- Neurotoxicity
  - Overstimulation
  - Tachycardia, hypertension
  - Muscle fasciculation
  - Cranial nerve dysfunction
  - Salivation
- Specific antivenin

Centipede Bites

- Front legs have venom
  - Potassium channel blocker
- Bites can be painful with edema
- Rare systemic reactions reported
- Ice packs best for pain
- Millipedes don't bite

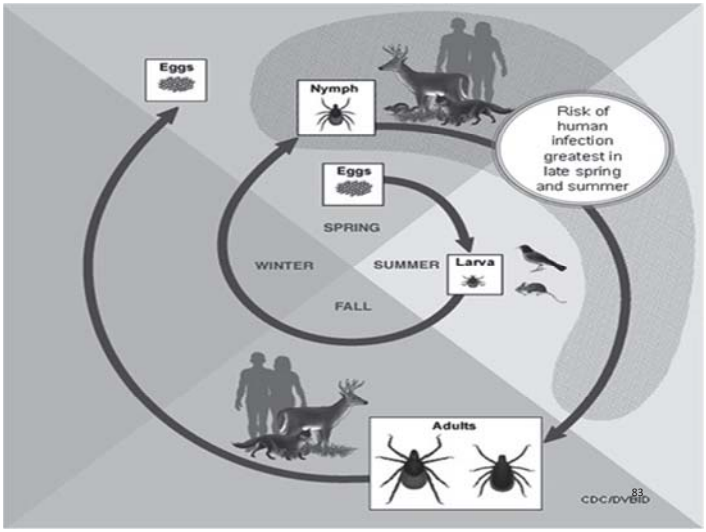
Ticks

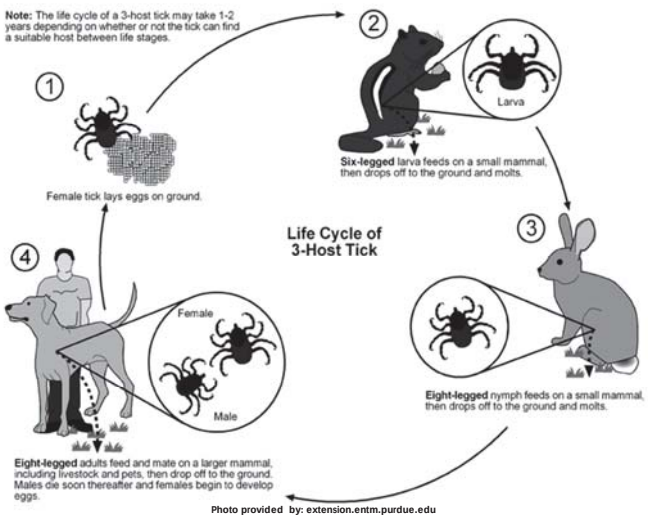
- Ubiquitous blood sucking parasites
- Prime spreader of infections



Tick Life Cycle

- Hard ticks have four life stages
  - Egg
  - Six-legged larvae
  - Eight-legged nymph
  - Adult
- Most ticks prefer to feed on different hosts at each life stage
- Ticks can feed on any land animal





J Am Acad Dermatol
June 2004

Safe Tick Removal

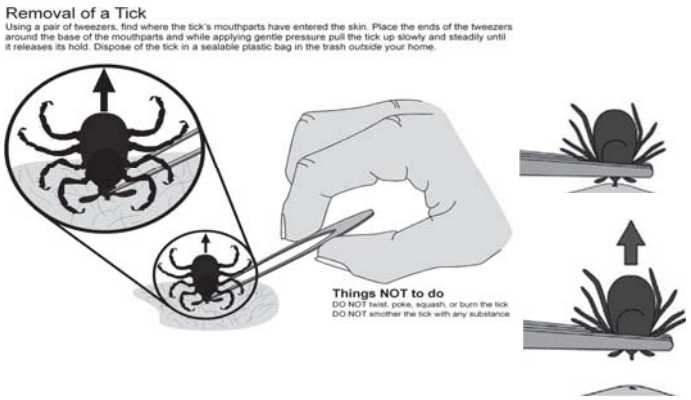


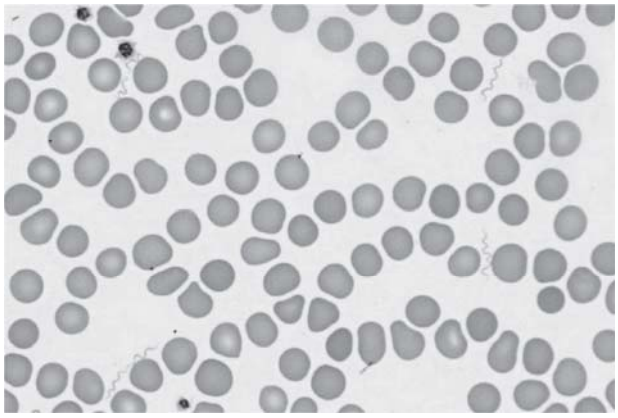
Photo provided by: extension.entm.purdue.edu

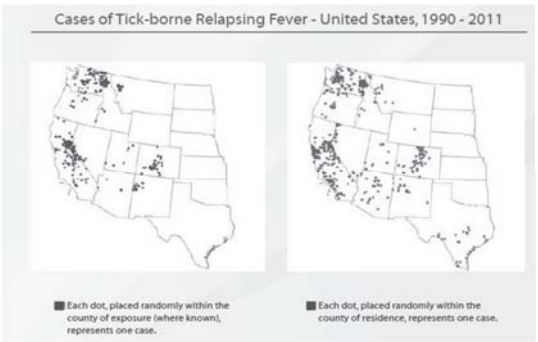
Tick Borne Disease

- Rickettsia
- Anaplasmosis/Ehrlichiosis
- Lyme disease
- Babesiosis
- Tularemia
- Relapsing Fever
- STARI
- Viral

Relapsing Fever

- Where it occurs
- Caused by: many spirochetes (a bacteria) species from the Borrelia genus
- Carried by: soft ticks of the Ornithodoros genus





Relapsing Fever

- Soft ticks
- Recurrent fevers
- Diagnosis by blood smear
- Treatment: Penicillin

Tick Paralysis

- NW and Rockies
- Caused by: a neurotoxin produced in the salivary glands of a female tick
- Carried by: deer tick, dog tick, Rocky Mtn. wood tick, and Lone Star tick

Tick Paralysis

- Ascending flaccid paralysis
  - Can start with ataxia
- Starts hours to day after bite
- Resolved in days to a week after tick removed

Meat Allergy

- Allergy to galactose-alpha-1,3-galactose (alpha-gal)
- Seen after tick bites
  - Lone star tick

Gila Monsters

- SW USA
- Can be up to 2 ft long
- Official state report of Utah
- Eats 5-10/year

Gila Monsters

- Only small amounts of venom
  - Drips into salvia
- Fatal bites children or idiots
- Very painful
- Rare reports of anaphylaxis
- Venom help developed GLP-1 agonist
  - Exenatide (Byetta)

Komodo Dragon

- Very large lizard
- Was thought to kill prey by inoculating them with bacteria leading to fatal sepsis
- Cultures showed mouth was a sewer of bacteria

But!

- Komodo same clade as Gila monsters
- Human bites with extensive bleeding
- Cultures only from captive animals

- **…and the anecdotal reports of persistent bleeding in human victims after bites (including B.G.F's personal observations)"**

Research

- **Komodo have venom glands and grooved teeth**
- **Killing pattern similar to Gila monster**
- **Cultures of wild animals mouths not that impressive**