



	Goals 
	<ul style="list-style-type: none"> ■ Learn diagnostic clues for “Can’t Miss Diagnoses” ■ Avoid “near misses” for these diagnoses ■ Learn which features of the history and physical examination are most useful to make correct diagnoses ■ Distinguish benign from potentially serious diagnoses ■ Risk scores and clinical decision tools ■ Pearls and pitfalls 

	Diagnostic Dilemmas
	<ol style="list-style-type: none"> 1. Does this patient have obstructive sleep apnea? 2. What is the cause of this patient’s night sweats? 3. Does this patient have temporal arteritis?

	Does This Patient Have Obstructive Sleep Apnea?

	Mr. Pickwick
	<ul style="list-style-type: none"> ■ 42 year old man ■ Notes poorer memory for 1 year ■ Distractable ■ Can’t multitask as well as before ■ What is the diagnosis? ■ How to proceed?

	Why is This Important?
	<ul style="list-style-type: none"> ■ 20-30% of U.S. men and 10-15% of women have at least mild obstructive sleep apnea (OSA) defined as AHI > 5 ■ High rates are paralleling obesity epidemic ■ Untreated OSA can decrease work productivity, cause daytime sleepiness, reduce quality of life, pose risk for traffic accidents ■ Effective treatment exists

	When Should You Consider? More than Just Daytime Somnolence...
	<ul style="list-style-type: none"> ■ Snoring ■ Witnessed apneas ■ Morning headaches ■ Attentional deficits and poor short term memory <ul style="list-style-type: none"> – Patients and providers may confuse for ADD ■ Resistant hypertension ■ Cor pulmonale <ul style="list-style-type: none"> – Peripheral edema – JVP elevation ■ Night sweats

Secondary (Identifiable) Causes of Hypertension: OSA More Common than Other Diagnoses Combined!

- Cushing's syndrome
- Renal artery stenosis
- Primary aldosteronism
- Pheochromocytoma
- Chronic kidney disease
- Coarctation of the aorta
- Thyroid or parathyroid disease
- Obstructive sleep apnea



Differential Diagnosis



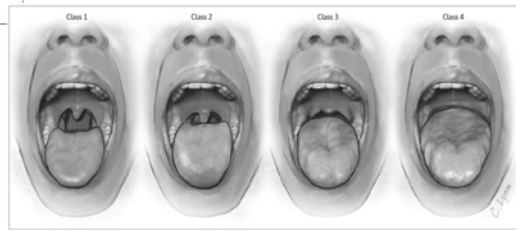
- Periodic leg movements of sleep
- Narcolepsy
- Central sleep apnea
- Neuromuscular disease of chest wall
- Attention deficit disorder
- GERD
- Nocturnal panic attacks
- Medical conditions causing chronic fatigue
- Ordinary insomnia

Which Aspects of History and Exam are Most Useful to Make Diagnosis (AHI > 10)?

Feature	Sensitivity	Specificity	LR+	LR-
History				
Hypertension	74%	45%	1.3	0.60
Nocturnal gasping	52%	84%	3.3	0.57
A.m. headache	22%	85%	1.5	0.92
Witnessed apnea	80%	42%	1.4	0.47
Daytime sleepiness	50%	61%	1.3	0.81
Exam				
Mallampati 3 or 4	55%	65%	1.6	0.68
Pharyngeal narrowing	67%	53%	1.4	0.63

Rational Clinical Exam JAMA 2013;310:731

Mallampati Classification



Class 1: Soft palate, uvula, pillars visible
 Class 2: Soft palate and base of uvula visible
 Class 3: Only soft palate visible
 Class 4: Only hard palate visible

Available Clinical Prediction Rules

- Berlin questionnaire (reference standard in research studies)
- STOP
- STOP-BANG
- Epworth Sleepiness Scale (ESS)
- Sleep apnea clinical score (SACS)

Which Clinical Prediction Rule? STOP-BANG

1. Do you snore loudly?
2. Do you often feel tired, fatigued, or sleepy?
3. Has anyone observed apneas during sleep?
4. High blood pressure?
5. BMI > 35
6. Age > 50
7. Neck circumference > 40 cm
8. Male gender

Total score ≥ 3

- High risk of OSA

- Sensitivity 87%

- Specificity 31%

Total score 5-8

- High risk for moderate to severe OSA (AHI > 10)

www.stopbang.ca

Confirmation of Value of STOP-BANG as a Screening Tool: Score of ≥ 3 Optimal

STOP BANG Score	Sensitivity %	Specificity %
≥ 1	100	2
≥ 2	98	20
≥ 3	91	52
≥ 4	76	71
≥ 5	54	84

Nagappa M, et al. PLoS One Dec. 2015

Pearls and Pitfalls



- Have a high index of suspicion
- Always consider OSA in differential diagnosis for ADD
- In resistant hypertension in obese patients, ask screening questions regarding possible OSA
- Consider OSA in scenarios beyond simply daytime somnolence

What is the Cause of This Patient's Night Sweats?

A Sweaty Man Sees You...

- 62 year old man
- Hypertension and type 2 diabetes
- 1 month of drenching night sweats and 5 pound weight loss
- What is the diagnosis?
- What is a rational approach to workup?

Why is This Important?



- Night sweats are common and often benign
- In one study, 41% of primary care office patients reported night sweats in past month including 23% with night sweats only (no daytime sweats)*
- Night sweats can be due to serious illness
- The challenge is to do "just the right amount" of workup for the right patients
- Minimize unnecessary testing, cost, and potential for false positive results

* J Fam Pract 2002;51:452

First Distinguish Between Four Overlapping Syndromes

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1. Flushing
 - Cutaneous vasodilatation
 - Redness in face and trunk apparent to others
2. Hot flashes
 - Warmth in face, neck, upper chest. Followed by sweating. Typical 5-15 minutes duration
3. Hyperhidrosis
 - Benign lifelong excessive sweating
4. Night sweats
 - Sweats requiring changing night clothes



Large Differential Diagnosis: How to Approach Differential Dx Rationally?	
Malignancy <ul style="list-style-type: none"> ■ Lymphoma ■ Germ cell tumors ■ Solid tumors Infections <ul style="list-style-type: none"> ■ Tb ■ Endocarditis ■ Osteomyelitis ■ HIV ■ Malaria 	Endocrine <ul style="list-style-type: none"> ■ Carcinoid ■ Hyperthyroidism ■ Pheo ■ Menopause Miscellaneous <ul style="list-style-type: none"> ■ Autonomic dysreflexia ■ Anxiety ■ Sleep apnea ■ Substance withdrawal

Smetana GW. UpToDate 2016

How Common are Night Sweats for the "Classic" Diagnoses?	
Smetana GW. UpToDate 2016	
Cause	Prevalence of Night Sweats
Hodgkin's Disease "B" symptom	25%
Pheochromocytoma	40%
Carcinoid syndrome	85%
Hyperthyroidism	50-90%
Menopause	35%
Infections	
• Tuberculosis	30-60%
• HIV / AIDS	10 to 70%
• Malaria	90%
Obstructive Sleep Apnea	25%

Medications May be One of Most Common Causes in Primary Care	
<ul style="list-style-type: none"> ■ Antidepressants ■ Triptans ■ GnRH agonists ■ Aromatase inhibitors ■ Sildenafil ■ Tamoxifen ■ Raloxifene 	<ul style="list-style-type: none"> ■ Insulin ■ Oral diabetic meds ■ Beta agonists ■ Alcohol ■ Niacin ■ Opioids ■ Aspirin ■ Tramadol

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Medications and Night Sweats: Particularly Remember Antidepressants as Cause	
Medication	Approximate Prevalence of Night Sweats
Antidepressants	
• SSRI antidepressants, bupropion	10-15%
• Tricyclics	15%
• Bupropion	>15%
Hormonal agents	
• Tamoxifen	65%
• Raloxifene	10-25%
• Anastrozole	5%
• Leuprolide	85%
Sildenafil and related drugs	10%
"Triptans" for migraine	3%

How to Distinguish Between Idiopathic Hyperhidrosis and Serious Cause?	
<ul style="list-style-type: none"> ■ First exclude fever <ul style="list-style-type: none"> – This changes and narrows differential diagnosis ■ Inquire about alarm features <ul style="list-style-type: none"> – Weight loss – Localized pain – IV drug use – High risk sexual history – High risk travel or country of origin – Known positive PPD 	

The History is the Most Important "Test" When Evaluating Night Sweats	
<ul style="list-style-type: none"> ■ Weight loss, fatigue, pruritus, lymphadenopathy – lymphoma ■ Localized pain – abscess, osteomyelitis, cancer ■ Back pain – cancer, endocarditis, epidural abscess or discitis ■ Risk factors for Tb – homeless, institutionalized, recent immigrant from endemic area, healthcare worker, known prior positive PPD ■ Recent new medications including OTC and complementary/alternative? ■ Flushing, diarrhea – carcinoid, hyperthyroidism ■ Characteristic hot flashes – menopause 	


	Focused Physical Exam to Seek Clues
	<ul style="list-style-type: none"> ■ Tachycardia, elevated bp – pheochromocytoma, hyperthyroidism ■ Lid lag, exophthalmos - hyperthyroidism ■ Lymphadenopathy – lymphoma, solid tumors, Tb, localized infection ■ Rales, rhonchi – Tb, pneumonia ■ Splenomegaly - lymphoma

	A Rational Approach to Testing if No Specific Diagnosis Suggested by History and Exam				
	<table> <tr> <th>Tier 1</th><th>Tier 2</th></tr> <tr> <td> <ul style="list-style-type: none"> ■ CXR ■ PPD ■ HIV antibody ■ CBC ■ TSH </td><td> <ul style="list-style-type: none"> ■ Blood cultures ■ Torso CT ■ +/- Gallium scan ■ Endocrine testing for pheo, carcinoid </td></tr> </table>	Tier 1	Tier 2	<ul style="list-style-type: none"> ■ CXR ■ PPD ■ HIV antibody ■ CBC ■ TSH 	<ul style="list-style-type: none"> ■ Blood cultures ■ Torso CT ■ +/- Gallium scan ■ Endocrine testing for pheo, carcinoid
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	Pearls and Pitfalls
	<ul style="list-style-type: none"> ■ No decision support tools available ■ Remember medications as a common cause of night sweats ■ Seek historical features that focus the subsequent workup ■ "Shotgun" labs only if no cause apparent after history and physical ■ Tier 2 studies only if Tier 1 studies normal, night sweats persist, and no cause suggested by history and exam

	Does This Patient Have Temporal Arteritis?

	Ms. Munch
	<ul style="list-style-type: none"> ■ 78 year old woman ■ Not usually a headache person ■ One month of bitemporal non-throbbing headaches ■ Non-disabling ■ Fatigue ■ Is this temporal arteritis?

	Why is This Important? 
	<ul style="list-style-type: none"> ■ Often overlooked ■ Incorrectly attributed to tension-type or cervicogenic headache ■ Potential for irreversible unilateral or bilateral visual loss if diagnosis missed ■ Prompt treatment with high dose prednisone nearly completely prevents subsequent visual loss

	When to Consider Temporal Arteritis? More than Just Headache... Any of Following if > 50 years old	WHEN?
	<ul style="list-style-type: none"> Any new onset persistent headache Does not need to be temporal Fever of unknown origin Acute visual loss Scintillating scotoma PMR symptoms 	<ul style="list-style-type: none"> Jaw claudication (true vascular claudication) Scalp tenderness Diplopia Mononeuritis multiplex Unexplained anemia High ESR not otherwise explained

	Differential Diagnosis
	<ul style="list-style-type: none"> Cervicogenic headache Tension-type headache TMJ dysfunction Migraine with aura Retinal detachment TIA

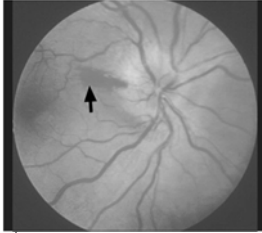
	Which Symptoms Best Predict Likelihood of Temporal Arteritis Among Patients Referred for Biopsy?																																																
	<table><tr><th>Symptom</th><th>Prevalence %</th><th>LR +</th><th>LR -</th></tr><tr><td>Anorexia</td><td>35</td><td>1.1</td><td>0.87</td></tr><tr><td>Weight loss</td><td>43</td><td>1.3</td><td>0.89</td></tr><tr><td>Diplopia</td><td>9</td><td>3.4</td><td>0.95</td></tr><tr><td>Fatigue</td><td>39</td><td>1.2</td><td>0.94</td></tr><tr><td>Fever</td><td>42</td><td>1.2</td><td>0.92</td></tr><tr><td>Temporal headache</td><td>52</td><td>1.5</td><td>0.82</td></tr><tr><td>Any headache</td><td>76</td><td>1.0</td><td>0.70</td></tr><tr><td>Jaw claudication</td><td>34</td><td>4.2</td><td>0.72</td></tr><tr><td>PMR</td><td>34</td><td>0.97</td><td>0.99</td></tr><tr><td>Unilateral visual loss</td><td>24</td><td>0.85</td><td>1.2</td></tr><tr><td>Vertigo</td><td>11</td><td>0.71</td><td>1.1</td></tr></table>	Symptom	Prevalence %	LR +	LR -	Anorexia	35	1.1	0.87	Weight loss	43	1.3	0.89	Diplopia	9	3.4	0.95	Fatigue	39	1.2	0.94	Fever	42	1.2	0.92	Temporal headache	52	1.5	0.82	Any headache	76	1.0	0.70	Jaw claudication	34	4.2	0.72	PMR	34	0.97	0.99	Unilateral visual loss	24	0.85	1.2	Vertigo	11	0.71	1.1
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	Abnormal Temporal Artery Exam is Most Useful Physical Finding to Predict Temporal Arteritis																																								
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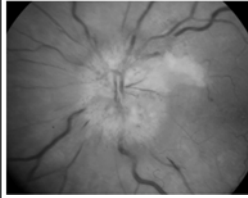
	Beaded and Prominent Temporal Arteries

Clinical Prediction Rule:					
Four Factors Most Specific for TA					
Young, et al. Mayo Clin Proc 2004;79:483					
	Headache	Jaw Claudication	Scalp tenderness	Visual Loss	LR+
1	✓				1.7
		✓			6.7
			✓		3.0
2	✓	✓			8.0
		✓	✓		17.0
	✓		✓		4.1
3	✓	✓	✓		15.0
	✓			✓	6.0
		✓		✓	6.0

Permanent Visual Loss due to Anterior Ischemic Optic Neuropathy: The Most Feared Complication



Arteritic AION with splinter hemorrhage



Arteritic AION with Disc Edema and Cotton Wool Spot

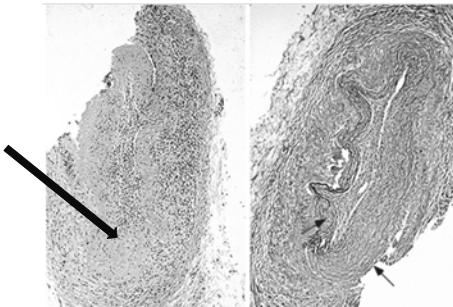
What to Do if Strong Suspicion for Temporal Arteritis?

- Prednisone 60 mg qd immediately (same day)
- Biopsy within 1 week optimal
- Biopsy within 2 weeks acceptable
- Biopsy same side as symptoms if unilateral
- Minimum optimal biopsy length 2 cm.
- If strong suspicion and biopsy negative, proceed to contralateral bx (up to 25% additional yield)

Pathologic Findings

Granulomatous and lymphocytic infiltration of wall of artery

Disruption of elastica



Pearls and Pitfalls



- Any new headache in patient over age 50 years, not just temporal headache
- Jaw Claudication and scalp tenderness most specific symptoms
- Abnormal temporal artery exam most useful physical finding
- A normal ESR makes TA much less likely (LR 0.2)
- Start prednisone immediately if TA suspected

Summary

- Certain features of the history and exam are more useful than others when distinguishing between benign and serious etiologies
- "Can't miss" diagnoses have characteristic clues
- Limited role for laboratory testing and imaging
- Clinical prediction rules and guidelines help for some, but not all, "can't miss" diagnoses