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Caution: Contents Under Pressure Identifying Drug-Induced Hypertension

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Caution: Contents Under Pressure Identifying Drug-Induced Hypertension

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Learning Objectives

Pharmacists

- Identify common challenges to achieving optimal blood pressure control
- Describe the complications of untreated hypertension
- Discuss the potential mechanisms of drug induced hypertension
- List drugs/supplements associated with secondary hypertension
- Given a patient case with hypertension, be able to recognize which medication is a potential causative agent

Technicians

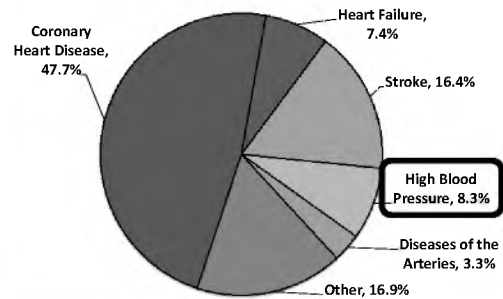
- Describe the complications of untreated hypertension
- List drugs/supplements associated with secondary hypertension

Why talk
about the
same old
thing...



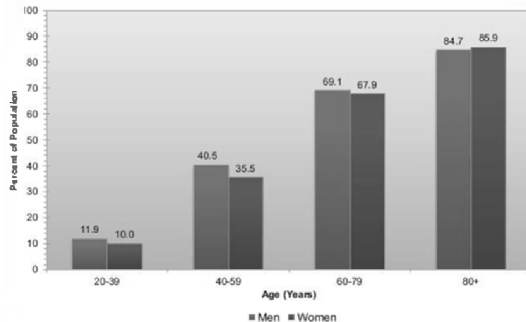
Images: <https://hachomecare.wordpress.com/>

Percentage of Deaths Attributable to Cardiovascular Disease (United States: 2011)

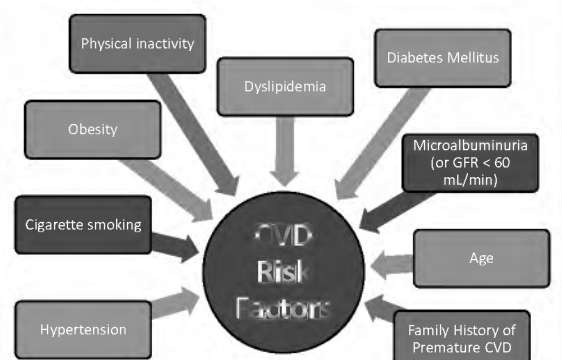


Adapted from Mozaffarian et al., *Circulation*, 2015;131:e29-e322

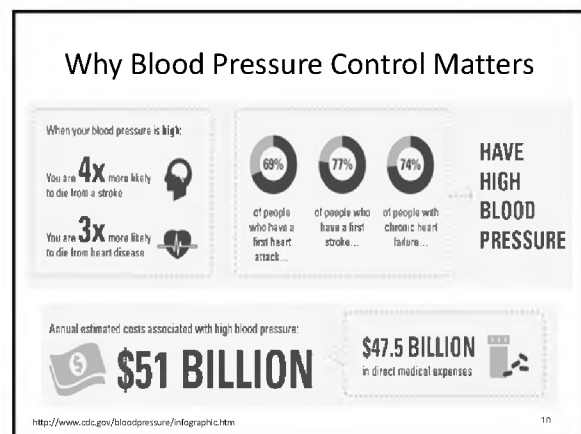
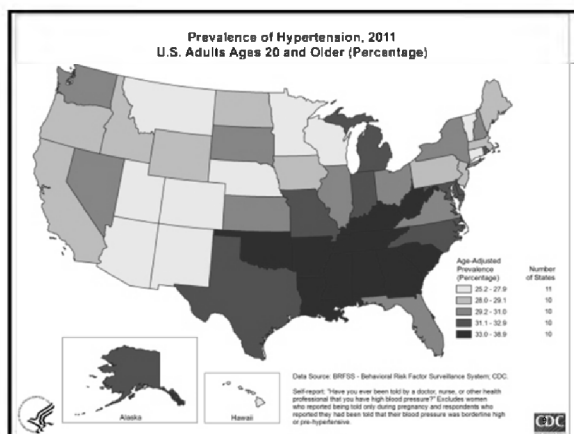
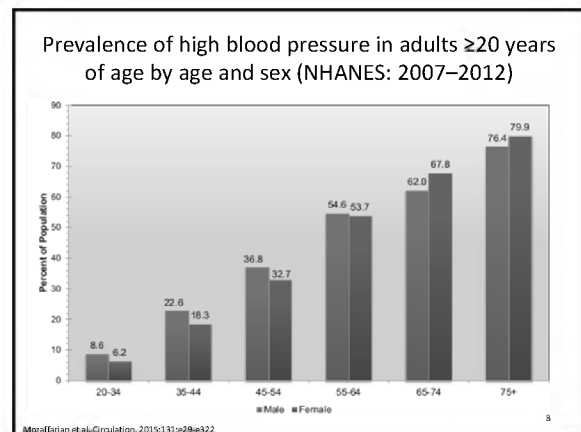
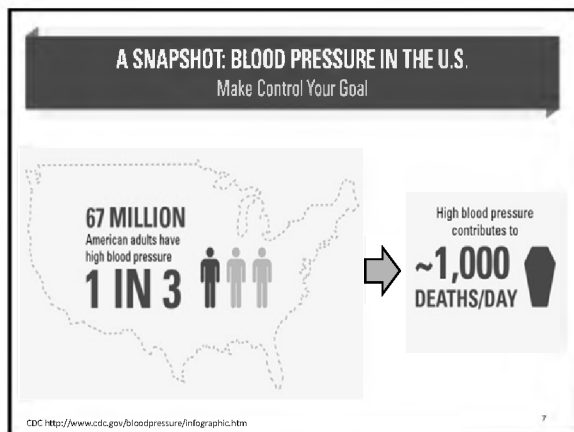
Prevalence of cardiovascular disease in adults ≥ 20 years of age by age and sex (NHANES: 2009–2012)



Mozaffarian et al., *Circulation*, 2015;131:e29-e322



Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (2003). (JNH Publication No. 03-5233). Bethesda, MD: U.S. Department of Health and Human Services. <http://www.hypertensioninfo.org>

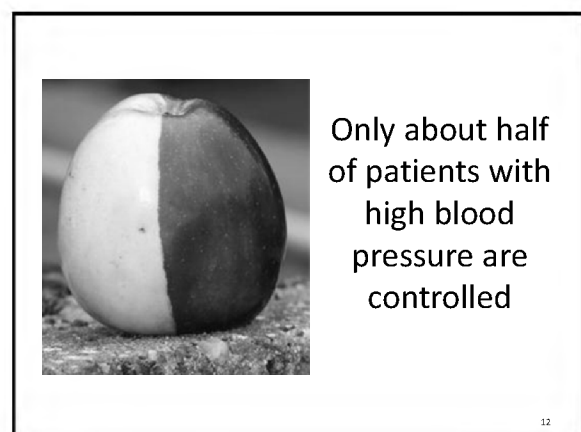


BP Control in the US

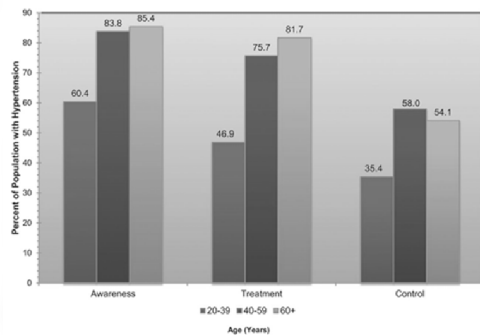
	NHANES 1976- 1980	NHANES 1988- 1991	NHANES 1991- 1994	NHANES 1999- 2000	NHANES 2007- 2012
Aware	51%	73%	68%	70%	83%
Treated	31%	55%	54%	59%	77%
Controlled	10%	29%	27%	34%	54%

SBP <140 mm Hg and DBP <90 mm Hg.
Age 18 to 74 years with SBP 140 mm Hg or DBP 90 mm Hg or taking antihypertensive medication.

JNC VI. *Arch Intern Med*. 1997;157:2413-46.
JNC VII. *JAMA*. 2003;289:2560-2572.
Mozaffarian et al. *Circulation*. 2015;131:e29-e322



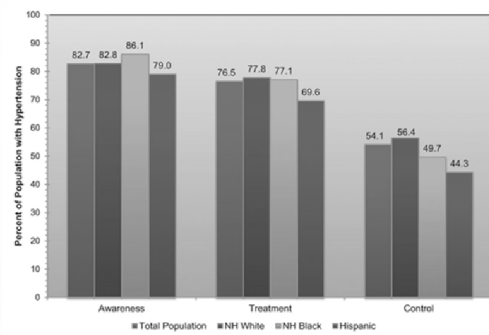
Extent of awareness, treatment, and control of high blood pressure by age (NHANES: 2007–2012)



Mozaffarian et al. Circulation. 2015;131:e20-e322

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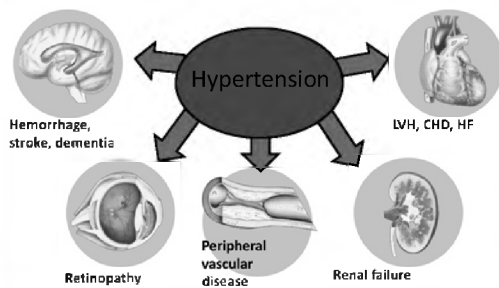
Extent of awareness, treatment, and control of high blood pressure by race/ethnicity (NHANES: 2007–2012)



Mozaffarian et al. Circulation. 2015;131:e20-e322

14

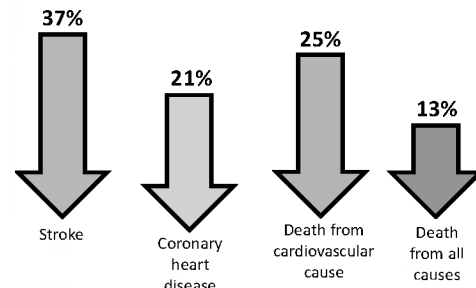
Target Organ Damage



Chobanian et al. JAMA. 2003;289:2560-2572

CHD, coronary heart disease

Reducing average population systolic blood pressure by only 12-13 mmHg could reduce:



CDC. <http://www.cdc.gov/bloodpressure/infographic.htm> Ogden LG, et al. Hypertension 2009; 35: 539-543. Chobanian, A. V. et al. Hypertension 2003;42:1206-1252; Habert Archives Int Med 1993; Moser, Am Coll Cardiol 1996

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Individual

Get Started

Preventing 1 Million Heart Attacks and Strokes: A Turning Point for Impact

Learn about Million Hearts® progress to date and actions you can take to help prevent 1 Million heart attacks and strokes.

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Audience Question:

A patient has blood pressure readings in the clinic that are consistently 136/84. How would you classify his blood pressure?

- Normal
- Pre-hypertension
- Stage 1 HTN
- Stage 2 HTN

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JNC VII Classification

BP Classification	SBP (mmHg)	DBP (mmHg)
Normal	<120	<80
Elevated	120-139	<80
Stage I Hypertension	140-159	90-99
Stage II Hypertension	≥160	≥95

Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (2003). JNC VII. <http://www.nhlbi.nih.gov/publications/jnc7>. Bethesda, MD: U.S. Department of Health and Human Services.

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Audience Question:

For the general population aged 60 years or older, the JNC 8 panel recommends initiating pharmacologic treatment to lower BP at a diastolic blood pressure of:

- 80
- 90
- 140
- 150

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Blood Pressure Goals

	JNC 7 (2003)	JNC 8 (2014)	ASH/ESH (2013)
Uncomplicated HTN	<140/90	<140/90	<140/90
Diabetes	<130/80	<140/90	<140/90
CVD	<140/90	--	<140/90
CKD	<130/80	<140/90	<140/90
Elderly	Not specified	<150/90 (≥60 years)	<150/90 (≥80 years)

JNC 8. JAMA. 2014;311(5):507-520.

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MAKE CONTROL YOUR GOAL EVERY DAY



Check your blood pressure regularly—at home, at a doctor's office, or at a pharmacy.



Quit smoking—or don't start. **1-800-CUT-NOW** or Smokefree.gov

Eat a healthy diet with:

- More fruits, vegetables, potassium, and whole grains
- Less sodium, saturated fat, trans fat, and cholesterol



Adults should limit alcohol to no more than:

- 1 drink per day for women
- 2 drinks per day for men



Nutrition Facts

- Read a serving label and lower your sodium intake
- Most of the sodium we eat comes from processed and restaurant foods
- About 90% of Americans eat too much sodium

Get active and maintain a healthy weight!



Aim for 2 hours and 30 minutes of moderate physical activity every week.

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Lifestyle Modifications

Modification	Approximate SBP reduction (range)
Weight reduction	5-20 mmHg/10 kg weight loss
Adopt DASH eating plan	8-14 mmHg
Dietary sodium restriction	2-8 mmHg
Physical activity	4-9 mmHg
Moderation of alcohol consumption	2-4 mmHg

Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (2003).

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Identifiable Causes of Hypertension

A	<ul style="list-style-type: none"> Accuracy Apnea Aldosteronism
B	<ul style="list-style-type: none"> Bruits (renovascular disease) Bad kidneys
C	<ul style="list-style-type: none"> Catecholamines Coarctation Cushing's syndrome
D	<ul style="list-style-type: none"> DRUGS Diet
E	<ul style="list-style-type: none"> Erythropoietin Endocrine disorders

Source: AAFP. 2014.

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Accuracy of Blood Pressure Measurement

- Equipment inspected
- Trained operator
- Patient properly positioned
- Caffeine, exercise, and smoking should be avoided for at least 30 minutes before
- Appropriately sized cuff
- Two measurements



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Definition of Drug-Induced Hypertension

High blood pressure caused by a response to using, or stopping the use of, a chemical substance, drug, or medication.

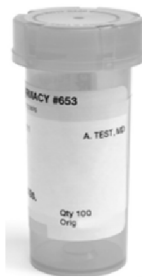
– U.S. National Library of Medicine/National Institutes of Health



<http://www.nlm.nih.gov/medlineplus/ency/article/000155.htm>

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Medication Adherence by the Numbers



For every 100 prescriptions written...

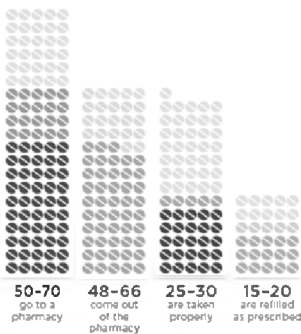


Image: http://millionhearts.hhs.gov/_docs/EP_Toolkit/TipSheet_MCP_MedAdherence.pdf

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Risk Factors for Drug-induced Hypertension

- History of elevated blood pressure
- Decreased GFR
- Metabolic syndrome
- Advanced age
- Persistent use of high dose NSAID therapy



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Audience Question:
Which of these medications is associated with increasing blood pressure?

- Cyclosporine
- Erythropoietin
- Indomethacin
- All of the above

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Drugs Associated with Increases in BP

Amphetamines	Bevacizumab	Bupirone	Caffeine
Celecoxib	Cocaine	Corticosteroids	Cyclosporine
Erythropoietin Stimulating Agents	Estrogen-containing oral contraceptives	Herbals	Licorice
Monoamine Oxidase Inhibitors	NSAIDS	Phenylephrine/Pseudoephedrine	Sibutramine (off market)
Sorafenib/Sunitinib	Tacrolimus	Testosterone	Venlafaxine

Mechanisms for Increasing BP

Volume retention	<ul style="list-style-type: none"> Glucocorticoids Hormones NSAIDs
Activation of the sympathetic nervous system	<ul style="list-style-type: none"> Decongestants Stimulants
Direct vasoconstriction	<ul style="list-style-type: none"> Cyclosporine Tacrolimus
Combined	<ul style="list-style-type: none"> Erythropoietin Alcohol VEGF
Unknown	

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Steroids/Glucocorticoids

- Occurs in at least 20% of patients
 - More in elderly and with family history
- Dose dependent
- Oral cortisol doses of 80-200 mg/day can increase systolic BP up to 15 mmHg in 24 hours
 - At low doses-cortisol has less effect
- Cessation usually results in normalization of BP
- Consider diuretic if long term steroid therapy needed



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Licorice



- Main ingredient-glycyrrhizic acid
- Excess mineralocorticoid
- Dose dependent
- Can have a sustained increase in BP

Images: <http://www.candyfavorites.com/candy-favorites/black-licorice>

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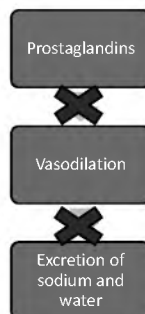
Estrogens (Oral Contraceptives)

- Induce HTN in ~5% of users
 - 50 mcg of estrogen and 1-4 mg of progestin
- Usually minimal but can be severe, even malignant HTN
- Risk decreases with cessation of oral contraceptive
- Postmenopausal HRT has minimal effect on BP-may even reduce
- If BP not controlled-may consider alternative contraceptive

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Nonsteroidal Anti-Inflammatory Drugs Cox-2 Inhibitors

- Ibuprofen, naproxen, piroxicam
- Celecoxib
- Implicated in increasing BP and CVD risk
- Can antagonize effects of some BP agents
- NSAIDs inhibit PG → vasoconstriction and volume retention
- Recommended
 - Monitor BP, renal function, and edema
 - Lifestyle changes and nonpharmacologic therapies for pain
 - Use lowest effective NSAID dose
 - Modifying antihypertensive therapy and diuretic management



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Change of BP in Hypertensives and Normotensives

	Hypertensive patients (mmHg)	Normotensive individuals (mmHg)
NSAIDs (pooled)	3.6-5.4	1.0-1.1
Indomethacin	4.8-6.0	1.0
Naproxen	3.1-6.1	ND
Piroxicam	2.9-6.2	ND
Sulindac	-1.6 to 2.2	-1.6
Aspirin	-1.8 to 1.0	0.6
COXIBs		
Rofecoxib	2.6-4.7	3.4
Celecoxib	-0.4	4.9

Armstrong, Clin Ther 2009

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Stimulants

- Nicotine, amphetamines
- Unpredictable
- Methylphenidate, amphetamines usually only cause modest increases
 - BP: 2-4 mmHg
 - HR: 3-6 bpm
- Some can experience significant increases in BP or HR

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Cocaine, Aesthetics, Narcotics

- Cocaine
 - Abuse causes adrenergic overactivity
 - Acute increases in BP, but not usually chronic increases
 - Problematic when used while taking beta blockers
- Ketamine
- Naloxone
 - Can acutely reverse antihypertensive effects of clonidine

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Decongestants

- Pseudoephedrine, phenylephrine, epinephrine, oxymetazoline, ephedra alkaloids
- Phenylpropanolamine-taken off market
- Mainly due to activation of the sympathetic nervous system
- Sympathomimetics with beta-blockers may increase BP due to unopposed alpha vasoconstriction

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Caffeine



- Potentially due to activation of the sympathetic nervous system
- More pronounced in males and African-Americans
- Caffeine in 2-3 cups of coffee can raise as much as 10 mmHg (average is 3-5 mmHg)
- Tolerance usually develops

Image: <http://www.theprospect.net/a/users/guide-to-caffeine-11237>

40

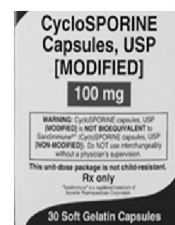
Antidepressants

- Venlafaxine-SNRI-3-13%
 - Meta-analysis-more pronounced
 - Dose dependent
 - Older patients
 - Men
- Monoamine oxidase inhibitors-selegiline
- Thioridazine-in overdose

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Immunosuppressive Agents

- Cyclosporine-BLACK BOX WARNING
 - Can be up to 30-80%
 - Can be mild to severe
 - Dose dependent
- Tacrolimus-associated much less than cyclosporine



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Recombinant Human Erythropoietin

- Reported to develop (or worsen) in 20-30% of patients
- May appear as early as 2 weeks and as late as 4 months
- Dose-related
- Increased risk
 - Pre-existing HTN, genetic predisposition, rapid risk in hematocrit

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Alcohol

- Excessive intake can raise BP
- Excessive alcohol can cause resistance to antihypertensives
- Studies find increase in prevalence of 7-11%
- Prospective cohort study
 - ~4,000 Japanese men
 - Greater in those who consume > 300 g/week
- Also can see HTN with disulfiram

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Anti-vascular Endothelial Growth Factor (VEGF) Signaling

- Bevacizumab
 - 8-18%
 - Dose related
 - More pronounced in elderly, preexisting HTN, renal cell carcinoma
- Sorafenib
- Sunitinib

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HAART

- May increase more than 10 mmHg (systolic or diastolic)
- Usually seen more with the therapy that causes metabolic changes (protease inhibitors)
 - Highest risk with lopinavir/ritonavir
 - Lower with atazanavir (rec in naïve patients)

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Other Herbal Products

- Yohimbine
 - Increases norepinephrine and sympathetic activation
 - Interacts with clonidine
- Ginseng
 - Information to suggest increase or decrease
- Ma huang/ephedra
 - Many case reports involving young adults
- Ginger
 - Seen with abuse of this agent
- St John's Wort

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American Heart Association
Life is why™
GETTING HEALTHY | CONDITIONS | HEALTHCARE / RESEARCH

IN THE NEWS

Evidence grows linking risk of stroke and marijuana
Smoking marijuana may increase the possibility of having a stroke, according to a review of 34 different studies.
Read more about marijuana and stroke.

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Conclusion

- Hypertension affects many Americans
- Controlling hypertension can help prevent complications
- In most cases, the cause of hypertension is unknown
- Identifying agents that can increase blood pressure can help patients to improve control
- All patients should follow lifestyle modifications

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Patient Case

- 76 year old female presents to the pharmacy with a new prescription for clonidine. She states "my doctor put me on another new medication to help control my blood pressure"
- Current medications: hydrochlorothiazide 25 mg daily, losartan 100 mg daily, metoprolol 50 mg twice daily, amlodipine 10 mg daily.
- She reports that her blood pressures at home are in the 150s on the top.

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- Current medications: hydrochlorothiazide 25 mg daily, losartan 100 mg daily, metoprolol 50 mg twice daily, amlodipine 10 mg daily.
- She reports that her blood pressures at home are in the 150s on the top.

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Patient Case (continued)

- When you question her about any medications that she takes OTC or supplements-she reports that she takes ibuprofen 3 tabs daily for her arthritis and ginger to help with her nausea.
- You also verify how (and if) she is taking all of her medications.
- What medications might be worsening her blood pressure?

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Strategies to Help with Adherence

- Simplify the regimen
- Impart knowledge
- Modify patients' beliefs and behavior
- Provide communications and trust
- Leave the bias
- Evaluate adherence

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- | | |
|---|---|
| S | • Simplify the regimen |
| I | • Impart knowledge |
| M | • Modify patients' beliefs and behavior |
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Contact Information

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