# Drugs that increase blood pressure

A number of drugs can increase blood pressure in individual subjects by degrees that may remain within the normal range, cause overt hypertension (BP > 140/90 mmHg), or even precipitate hypertensive crises. Such blood pressure increases are often potentiated by coexisting cardiovascular conditions, renal disease, diabetes, obesity and interactions with other concomitant medications. The need to investigate for the presence of drugs that may be contributing to elevated blood pressures or impairing responses to antihypertensive medications has been emphasized, particularly in the evaluation of resistant and refractory hypertension. Antihypertensive effects of diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and β-blockers may be blunted. The drugs most commonly associated with blood pressure elevations are nonsteroidal anti-inflammatory agents, sympathomimetic amines, estrogen-containing oral contraceptives, herbal preparations such as ephedra, certain antidepressants and immunosuppressants. Although most drug-induced blood pressure increases do not, in fact, lead to hypertension, systolic and diastolic blood pressure elevations of as little as 2 mmHg lead to significant increases in the risk of cardiovascular events. When a medication with the potential to increase blood pressure is added to a patient's therapeutic regimen, it is necessary to recognize that potential, and imperative to monitor possible changes in blood pressure even within the normal range.

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Discussions of hypertension management are invariably directed toward an understanding of the mechanisms and uses of antihypertensive drugs. What is often lost in these considerations is the possibility that concomitant drugs may be contributing to blood pressure elevations in individual situations. The need to investigate for the presence of drugs that may be contributing to elevated blood pressures or impairing responses to antihypertensive medications has been emphasized in the Joint National Committee (JNC) 7 report [1]; such considerations are particularly important in the evaluation of resistant and refractory hypertension [2]. The intent of this article is to provide a focused review of those agents currently best documented to increase blood pressure; more extensive lists and discussions are available [2–4].

One issue that often escapes attention and is therefore an extremely important consideration is the so-called 'iceberg effect', a very common situation in which a drug may significantly increase blood pressure while the blood pressure remains in the 'normal range' as outlined by JNC 7 criteria. In clinical trials in which blood pressure is not a primary end point but rather a safety parameter, measurements are less carefully collected and are generally qualitative rather than quantitative, lacking carefully matched control data. Many reports simply describe new 'hypertension' (≥140/90 mmHg) rather than significant increases within the 'normal range.' However, each blood pressure increase of 20/10 mmHg, even at blood pressures <140/80 mmHg, doubles the cardiovascular event rate [5], and small but significant differences in event rates can be demonstrated between 'high normal' and 'optimal' blood pressures [6]. Yet another consideration is that accentuated blood pressure responses are often observed in the presence of older age and coexisting cardiovascular or renal disease.

The more important drug classes and individual drugs demonstrated to increase blood pressure are listed in TABLE 1; the more significant of these are discussed in more detail in this article. Categorization of these drugs is difficult in that they may be represented in more than one class; as an example, sympathomimetic agents may be considered as decongestants, stimulants and weight-loss medications. It is important to recognize that not all agents within a class have the same effects upon blood pressure. A prime example of this is the cholesteryl ester transfer protein (CETP) inhibitor torcetrapib; while this drug was withdrawn from clinical trials owing to

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**Table 1. Oral agents that increase blood pressure.**

| Category | Examples |
| --- | --- |
| Anabolic steroids | Norandrolone, oxymetholone, oxandrolone |
| Antidepressants | Venlafaxine, tricyclics, MAO inhibitors |
| Antiobesity drugs | Sibutramine, phentermine |
| CETP inhibitors | Torcetrapib |
| Erythropoietin | rHuEPO, darbepoetin |
| Herbal preparations | Ephedra |
| Immunosuppressants | Cyclosporin, tacrolimus |
| Mineralocorticoids | Licorice, carbenoxolone, fludrocortisone, 9α-fluoroprednisolone |
| NSAIDs/coxibs | All, but COX-2 worse than COX-1, indomethacin |
| Oral contraceptives | Estrogen containing |
| Serotonergics (antimigraine) | Dihydroergotamine, sumatriptan |
| Stimulants | Methylphenidate, dexmethylphenidate, dextroamphetamine, amphetamine, methamphetamine, modafinil |
| Sulfonylureas | Glibenclamide |
| Sympathomimetic amines | Catecholamines and analogs, phenylpropanolamine |

CETP: Cholesteryl ester transfer protein; COX: Cyclooxygenase; MAO: Monoamine oxidase; rHuEPO: Recombinant human erythropoietin.

a significant increase in blood pressure resulting from an increase in aldosterone levels [7], newer drugs in this class, such as anacetrapib, appear devoid of blood pressure issues [8].

## NSAIDs

Perhaps the most widely recognized examples of drugs that can cause hypertension are the NSAIDs, including the cyclooxygenase (COX)-2 specific inhibitors (coxibs). There has been considerable discussion as to possible differences among these drug classes as well as drugs within each class relative to the danger of induced blood pressure elevations. As early as 1994 a meta-analysis using eight databases from 50 randomized trials demonstrated that NSAIDs elevated supine mean blood pressure by an average of 5.0 mmHg (95% confidence interval [CI]: 1.2–8.7 mmHg), and antagonized the antihypertensive effect of β-blockers (blood pressure elevation: 6.2 mmHg; CI: 1.1–11.4 mmHg) [9]. Among NSAIDs of the COX-1 class, piroxicam produced the most marked elevation in blood pressure (6.2 mmHg; CI: 0.8–11.5 mmHg), whereas sulindac and aspirin had the least hypertensive effect. Among 19 randomized controlled trials involving coxibs published before May 2004, with a total of 45,451 participants, coxibs increased systolic/diastolic blood pressure compared with placebo (3.85/1.06 mmHg) and nonselective NSAIDs (2.83/1.34 mmHg) [10]. In this analysis coxibs were associated with a nonsignificantly higher relative risk (RR) of causing hypertension compared with placebo (RR: 1.61; CI: 0.91–2.84; p = 0.10) and NSAIDs (RR: 1.25; CI: 0.87–1.78; p = 0.23). Rofecoxib increased systolic blood pressure by 2.83 mmHg and caused a nonsignificantly higher risk of developing clinically important systolic blood pressure elevation (RR: 1.50; CI: 1.00–2.26; p = 0.05) compared with celecoxib.

The relative blood pressure effects of rofecoxib and celecoxib were compared in 1092 subjects aged ≥65 years of age with osteoarthritis and receiving a fixed antihypertensive regimen [11]; significantly more patients in the rofecoxib group developed increased systolic blood pressure, defined as an increase >20 mmHg with an absolute value ≥140 mmHg at any time point (14.9 vs 6.9%; p < 0.01). The greatest increase in systolic blood pressure caused by rofecoxib occurred in patients receiving angiotensin-converting enzyme inhibitors (ACEIs) or β-blockers, whereas those on calcium channel antagonists or diuretic monotherapy receiving either celecoxib or rofecoxib showed no significant increases in blood pressure. In another trial, celecoxib was compared with rofecoxib and naproxen in Type 2 diabetes patients on stable antihypertensive regimens including ACEI or angiotensin receptor blockers (ARBs) using 24-h ambulatory blood pressure monitoring [12]. The mean ± standard error 24-h systolic blood pressure following 6 weeks of therapy was increased significantly by rofecoxib (130.3 ± 1.2 to 134.5 ± 1.4 mmHg; p < 0.001) but not by celecoxib (132.0 ± 1.3 to 131.9 ± 1.3 mmHg; p = 0.54) or naproxen (133.7 ± 1.5 to 133.0 ± 1.4 mmHg; p = 0.74). The blood pressure difference between rofecoxib and celecoxib was 3.78 mmHg (CI: 1.18–6.38 mmHg; p = 0.005); between rofecoxib and naproxen, 3.85 mmHg (CI: 1.15–6.55 mmHg; p = 0.005). A total of 30% of patients receiving rofecoxib with controlled blood pressure at baseline developed hypertension (p = 0.05), compared with 16% receiving celecoxib (p = not significant [NS]) and 19% receiving naproxen (p = NS).

The blood pressure effects of NSAIDs presumably occur secondary to inhibition of renal prostaglandin production, especially prostaglandins $E_2$ and $I_2$, with subsequent sodium and fluid retention [13]. Elderly patients, diabetics and patients with chronic kidney disease are at increased risk of manifesting these adverse effects. Rofecoxib exhibited the greatest increase in adverse cardiovascular events and has been withdrawn from the market [14].

Not only can both NSAIDs and coxibs increase blood pressure, but they can blunt the blood pressure lowering effects of several antihypertensive medication classes, including diuretics, ACEIs, ARBs and β-blockers [15–17]. This is an important factor in the assessment of causes of resistant hypertension.

## Sympathomimetic amines (decongestants/stimulants/diet drugs)

Sympathomimetics are vasoactive amines that increase blood pressure by direct activation of the sympathetic nervous system. The effects of the sympathomimetic amines pseudoephedrine and phenylpropanolamine on blood pressures, as evaluated by MEDLINE, EMBASE and the Cochrane Library searches of randomized placebo-controlled trials of treatment in adults, have been published [18,19]. Pseudoephedrine (24 trials with 45 treatment arms; 1285 patients) caused a small but significant increase in systolic blood pressure (0.99 mmHg; CI: 0.08–1.90 mmHg) and heart rate (2.83 bpm; CI: 2.0–3.6 bpm), with no effect on diastolic blood pressure (0.63 mmHg; CI: -0.10–1.35 mmHg). Patients with controlled hypertension experienced a systolic blood pressure increase of similar magnitude (1.20 mmHg; CI: 0.56–1.84 mmHg) [18]. Phenylpropanolamine (33 trials reporting 48 treatment arms with 2165 patients) increased systolic blood pressure by 5.5 mmHg (CI: 3.1–8.0 mmHg) and diastolic blood pressure by 4.1 mmHg (CI: 2.2–6.0 mmHg) with no effect on pulse rate. Patients with controlled hypertension were not at greater risk of blood pressure elevation. Individual responses varied widely; 18 studies contained at least one treated subject having blood pressure elevations ≥140/90 mmHg, an increase in systolic blood pressure ≥15 mmHg or an increase in diastolic blood pressure ≥10 mmHg. The hypertensive effects of these sympathomimetic amines were in general more pronounced with shorter-term administration, higher doses of medication, and immediate release formulations [19]. Similar drugs with the potential to increase blood pressure are pseudoephedrine, phenylephrine, oxymetazoline and naphazoline.

Modafinil, a psychostimulant widely used to attenuate fatigue and promote wakefulness, substantially alters autonomic cardiovascular regulation and increases heart rate and blood pressure [20]. Modafinil increased resting heart rate (9.2 ± 2.0 bpm; CI: 4.7–13.6 bpm; p = 0.001), resting systolic blood pressure (7.3 ± 3.2 mmHg; CI: 0.2–14.4 mmHg; p = 0.044), and resting diastolic blood pressure (5.3 ± 1.7 mmHg; CI: 1.4–9.1 mmHg; p < 0.012), and increased plasma and urinary catecholamines in 12 healthy hospitalized normal subjects.

## Antiobesity drugs

Observations of blood pressure changes with the weight-loss drug sibutramine, also recently removed from the market owing to induced blood pressure increases, illustrate the difficulty with blood pressure assessment. Although sibutramine did not in general augment blood pressure in stage 1 or stage 2 hypertension or isolated systolic hypertension, marked standard deviations were noted with several markedly hypertensive responses, thus indicating the variability of individual responses [21]. Over-the-counter (OTC) weight-loss preparations will be discussed in the section on 'Herbal supplements'.

## Sulfonylureas

At least some of the sulfonylurea agents may negatively interfere with blood pressure control, sympathetic activity and plasma insulin level, as illustrated in the following study [22]. A total of 48 Type 2 diabetic, hypertensive and hyperlipidemic subjects receiving an ACEI and a statin were randomized into two groups to receive the thiazolidinedione rosiglitazone or the sulfonylurea glibenclamide. The rosiglitazone group experienced a significant drop in systolic/diastolic blood pressure (6.1 ± 4.1/4.2 ± 1.9 mmHg); however, the glibenclamide group showed an increase in systolic blood pressure (3.1 ± 2.5 mmHg), no change in diastolic blood pressure, significant elevation in plasma insulin concentration by 2.3 ± 1.4 mu/l and augmentation of sympathetic activity. Glibenclamide worsened blood pressure control possibly by elevation of insulin levels and activation of the sympathetic nervous system, while rosiglitazone improved both plasma glucose and blood pressure levels, possibly by attenuation of hyperinsulinemia and sympathetic nervous system activity. Glibenclamide has been reported to directly affect the vascular smooth muscle potassium-dependent ATP channel, an action that may well increase vascular tone and reduce vasodilatory activity; this may represent another possible mechanism for the observed effects [23].

## Oral contraceptives

Most studies on blood pressure in normotensive women have shown an increase in blood pressure associated with oral contraceptive (OC) use. In a prospective cohort study in the USA, 68,297 female nurses aged 25–42 years and

free of diagnosed hypertension, diabetes, coronary heart disease, stroke and cancer at baseline were followed up for 4 years [24]; during 231,006 person-years of follow-up, 1567 incident cases of hypertension were diagnosed. A review of two studies found an average increase in systolic blood pressure by 7–8 mmHg compared with those not using OCs [25,26]. Compared with women who had never used OCs, the OC produced a significant increase in 24-h ambulatory systolic blood pressures (from 120 ± 3/75 ± 2 to 128 ± 4/81 ± 2 mmHg; p < 0.04), which was particularly evident for night-time values (from 108 ± 2/64 ± 2 to 120 ± 4/73 ± 2 mmHg; p < 0.02); two normotensive women became hypertensive [25]. The newer progestins, such as drospirenone, with antimineralocorticoid diuretic effects, lower blood pressure [27]. Mildly hypertensive subjects taking low dosage estrogen-progestogen OCs exhibited significantly higher daytime and night-time systolic blood pressure values as recorded by ambulatory blood pressure monitoring compared with hypertensive controls not taking OCs [26]; an average 8.3 mmHg difference (CI: 3.0–13.7 mmHg; p = 0.003) for the daytime and 6.1 mmHg difference (CI: 0.4–11.8 mmHg; p = 0.04) for the night-time was reported. These data indicated that hypertensive OC users with the same office blood pressure as that in hypertensive non-contraceptive users have a significantly higher ambulatory systolic blood pressure.

## Anabolic androgenic steroids

Analysis of data from 49 studies describing 1467 athletes using anabolic androgenic steroid (AAS) linked drug use with elevated systolic and diastolic blood pressure and with left ventricular hypertrophy that may persist after drug cessation [28]. One small study evaluated the effects of AAS administration in combination with resistance training on blood pressure in male amateur bodybuilders as compared with the results in a morphologically matched, resistance trained control group before, during and after the AAS cycle [29]. Significant increases in both diastolic and mean arterial blood pressures that remained within the normal range were found in the AAS group and returned to normal baseline measurements between 6 and 8 weeks postcycle.

## Erythropoietin

Recombinant human erythropoietin (rHuEPO) has been reported to induce hypertension [30].

When 41 patients receiving hemodialysis (HD) and 36 patients with predialysis (CRF) receiving intravenous injection of rHuEPO were compared, mean blood pressure was increased significantly in HD patients, but not in CRF patients (HD: 103 ± 5 to 105 ± 6 mmHg, p < 0.05; CRF: 103 ± 4 to 103 ± 6, p = NS). The percentage of patients with increased mean blood pressure >10 mmHg after rHuEPO injection was significantly larger in the HD than in the CRF group (27.0 vs 5.5%; p < 0.01). A positive correlation was found between changes in endothelin-1 level and mean blood pressure in the HD (r = 0.43; p < 0.01) but not in predialysis chronic renal failure.

## Herbal supplements

There is a most definite lack of adequate clinical information concerning the efficacy and safety of herbal products and few systematic clinical trials adequate to define the specific cardiovascular effects of individual herbal agents; most are available as OTC preparations. Many people with hypertension and cardiovascular diseases take such agents, do not consider them drugs and hence do not consider it important to inform their physicians that they are using such OTC agents [31]. The complicated issues surrounding the toxicity of herbal preparations have recently been extensively reviewed [32]. As discussed in this review, such supplements may cause not only blood pressure elevations but a variety of additional adverse cardiovascular effects. Herbal stimulants, including bitter orange, ephedra, caffeine, guarana, maté, kola, areca, lobelia and khat appear to be the more common offenders. Contributing to the problem is the fact that supposedly 'herbal' products are often adulterated with prescription drugs such as anorectics, antidepressants, diuretics or phosphodiesterase-5 inhibitors that are not listed on their labels [32]. Herbal ingredients may cause significant interactions with prescription drugs; as an example, *Ginkgo biloba* causes raised blood pressure when combined with a thiazide diuretic [33].

Ephedra alkaloids (ma huang) have a considerable potential to increase blood pressure [34,35]. The combination of caffeine with ephedra in dietary supplements appears to be particularly likely to increase systolic blood pressure; a randomized controlled trial found an increase in systolic blood pressure of 124 ± 12 mmHg relative to 119 ± 10 mmHg (p = 0.009) in supplement users compared with placebo subjects [36].

Hypertensive encephalopathy has also been reported following use of OTC products containing a mixture of ephedra and caffeine alkaloids [37]. Yohimbine, an alkaloid with stimulant and aphrodisiac effects found naturally in *Pausinystalia* and *Rauwolfia serpentina* (Indian Snakeroot), is an $\alpha_2$-adrenergic receptor antagonist that increases blood pressure by increasing plasma norepinephrine release from sympathetic nerve terminals and epinephrine release from the adrenal glands [38]. Licorice, containing the active ingredient glycyrrhizin, available in not only candy and oral tobacco products but also a wide variety of herbal products, can raise blood pressure by suppressing the metabolism of cortisol, resulting in increased stimulation of the mineralocorticoid receptor [39].

## Antidepressants

Antidepressant drugs act by altering brain catecholamine concentrations, the result of which may be an increase in blood pressure. Blood pressure effects of antidepressants vary widely among classes (Table 2). A study that reviewed data from 2028 depressed subjects reported that users of tricyclic antidepressants had higher mean systolic and diastolic blood pressures and were more likely to have hypertension stage 1 (RR: 1.90; CI: 0.94–3.84; p = 0.07) and stage 2 (RR: 3.19; CI: 1.35–7.59; p = 0.008) [40]. The combined reuptake inhibitor and receptor blocker mirtazapine is 50% less likely to cause hypertension and tachycardia than the tricyclic agents [41]. Newer reversible monoamine oxidase inhibitors, including moclobemide and brofaromine, appear less problematic for blood pressure than the nonreversible inhibitors, such as phenelzine and clorgyline [42]. Users of noradrenergic and serotonergic working antidepressants were more likely to have stage 1 hypertension. However, extended release venlafaxine has been reported to cause hypertension in 12.5% of patients receiving high doses [43,44].

## Steroids & immunosuppressants

Glucocorticoids, such as prednisone, induce sodium and fluid retention and can result in significant increases in blood pressure [45]. Those corticosteroids with the greatest mineralocorticoid effect, such as cortisone and hydrocortisone, produce the greatest amount of fluid retention. Blood pressure increases are further augmented in the presence of concomitant immunosuppressive therapy. A published search of the Cochrane Database of Systematic

### Table 2. Blood pressure effects of antidepressant drugs.

| Class | Examples | Blood pressure effect |
|---|---|---|
| SSRIs | Citalopram, escitalopram, fluoxetine, paroxetine, sertraline | No change |
| Tricyclics | Amitriptyline, desipramine, imipramine, nortriptyline | Increase |
| SNRIs | Venlafaxine, duloxetine | Greater increase |
| NDRIs | Bupropion | No change |
| CRIRBs | Trazodone, nefazodone, maprotiline, mirtazapine | Increase, no change |
| MAO | Phenelzine, tranylcypromine | Increase |

*Association of hypertension with depression makes these data very difficult to quantitate.*
*CRIRB: Combined reuptake inhibitors and receptor blocker; MAO: Monoamine oxidase inhibitor; NDRI: Norepinephrine–dopamine reuptake inhibitor; SNRI: Serotonin–norepinephrine reuptake inhibitor; SSRI: Selective serotonin reuptake inhibitor.*

Reviews identified 17 trials adequate for analysis of the hypertensive effects of cyclosporine [46]; a highly statistically significant increase in blood pressure was associated with cyclosporine use in a dose-dependent relationship. Lower doses (1–4 mg/kg/day) increased mean blood pressure by an average of 5 mmHg and higher doses (>10 mg/kg/day) by 11 mmHg. Tacrolimus, like cyclosporine, has been shown to have a significant effect on blood pressure. However, the incidence of tacrolimus-induced hypertension (35%) is less than that of cyclosporine (50%) [47]. The mechanisms underlying cyclosporine/tacrolimus-induced hypertension are complex and include altered vascular endothelial function; vasodilators such as prostacyclin and nitric oxide are suppressed and vasoconstrictors, including endothelin, are increased [48]. Insulin resistance is also increased [49].

## Conclusion

Many drugs and herbal agents increase blood pressure. Increases are often potentiated by coexisting cardiovascular conditions and drug interactions. Most increases remain under the radar and within the 'normal' range (<140/90 mmHg). While a small increase in blood pressure within the normal range may be difficult to detect, such an increase is important. However, any increase in blood pressure increases cardiovascular risk; small changes should be evaluated on a risk–benefit basis. Thus, it is imperative to monitor for possible changes in blood pressure when a medication with the potential to increase blood pressure is added to a patient's therapeutic regimen. Increases into the 'hypertensive' range, and even hypertensive crises, are not uncommon. Careful attention to possible effects of concomitant medications upon blood pressure is essential.

## Future perspective

There is increasing emphasis on recognition of the critical importance of blood pressure control; more aggressive treatment targets are being proposed. It is imperative to recognize confounding patient issues that result in resistant and even refractory hypertension. Furthermore, recognition that even small increases in systolic and diastolic blood pressures within the 'normal range' (<140/90 mmHg), especially in high cardiovascular risk groups, such as those with diabetes, will direct more attention to identification of medication-induced blood pressure increase or resistance to antihypertensive drug efficacy. This will require careful attention to appropriate blood pressure measurement during clinical trials of all drugs, not only those with expected blood pressure altering effects. Physicians and physician extenders will be expected to monitor patients carefully for use not only of prescribed drugs but of OTC/herbal drugs as well, and to consider the potential for medication-induced blood pressure increases, even if only small. When a new medication with known potential for blood pressure increase is prescribed, it will become increasingly important for monitoring for blood pressure increases. Furthermore, the decision to prescribe drugs with known potential for blood pressure increases, such as NSAIDs, should be made on a risk–benefit basis, and the blood pressure monitored closely.

## Financial & competing interests disclosure

## Executive summary

### Drugs that increase blood pressure
- Many medications, both prescription drugs, over-the-counter (OTC) drugs and herbal preparations can increase blood pressure significantly, causing not only small increases in both systolic and diastolic pressure within the normal range, but overtly hypertensive responses as well.

### Nonsteroidal anti-inflammatory drugs
- Both nonsteroidal anti-inflammatory drugs and coxibs can not only increase blood pressure, but also blunt the antihypertensive effects of medications such as β-blockers, diuretics, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers.

### Sympathomimetic amines
- Sympathomimetic amines, such as pseudoephedrine, phenylpropanolamine and oxymetazoline, are potent vasoconstrictors readily available as OTC decongestants and can profoundly increase blood pressure, particularly when used at higher doses.

### Antiobesity drugs
- Hypertensive responses have caused drugs, such as sibutramine, to be removed from the market; however, OTC weight-loss preparations often contain herbal products and even prescription drugs not listed on their labels that may increase blood pressure.

### Sulfonylureas
- Drugs of this class, particularly glibenclamide, may increase sympathetic nervous system activity and increase at least systolic blood pressure.

### Oral contraceptives
- Estrogen–progesterone oral contraceptives can elevate blood pressure, particularly ambulatory daytime and night-time pressures; however, newer progestin agents actually lower blood pressure.

### Anabolic androgenic steroids
- The limited data available on the hemodymanic effects of anabolic androgenic steroids indicate that they may increase both systolic and diastolic blood pressure and contribute to left ventricular hypertrophy.

### Erythropoietin
- Recombinant human erythropoietin can increase blood pressure in dialysis patients by more than 10 mmHg, possibly by increasing endothelin plasma levels.

### Herbal supplements
- There is clearly a lack of adequate clinical information as to the safety of herbal products; however, ephedra alkaloids, particularly when combined with caffeine, may cause a large increase in systolic blood pressure and even hypertensive encephalopathy.

### Antidepressants
- Tricyclics and venlafaxine appear to have the greatest propensity to increase blood pressure.

### Steroids & immunosuppressants
- Glucocorticoids increase blood pressure primarily by salt and water retention; cyclosporine and tacrolimus increase blood pressure in a dose-dependent manner.

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