Hypertension in preeclampsia. Although the mechanism of the increased blood pressure in preeclampsia is not established, evidence suggests it may involve multiple processes. A possible scenario involves the following: decreased placental production of estrogen and progesterone, both of which have hemodynamic effects; increased circulating endothelial toxins, possibly released from a poorly perfused placenta; and increased activity of the sympathetic nervous system. These processes may then result in alterations in platelet-vascular endothelial cell function, with decrease in vasodilators such as nitric oxide and prostacyclin and increased production of vasoconstrictors such as endothelin (ET). Compensatory suppression of the renin-angiotensin system occurs, suggesting that excess angiotensin II (AII) does not play a major role in preeclamptic hypertension (HT). Finally, sodium retention owing to renal vasoinhibition may further increase blood pressure.

Compensatory responses:
- Plasma renin
- Aldosterone

Figure 10-32

Light microscopy of the renal lesion of preeclampsia: glomerular endotheliosis. On light microscopy, the glomeruli from preeclamptic women are characterized by swelling of the endothelial and mesangial cells. This swelling results in obliteration of the capillary lumina, giving the appearance of a bloodless glomerulus. On occasion, the mesangium, severely affected, may expand. Thrombosis and fibrinlike material and foam cells may be present, and epithelial crescents have been described in rare instances [2].

Figure 10-33

Functional renal alterations in preeclampsia. The functional consequences of glomerular endotheliosis and of the hormonal alterations in preeclampsia are summarized in this schematic diagram of the nephron in preeclampsia. Suppression of the renin-angiotensin system occurs, probably in response to vasoconstriction and elevated blood pressure. The glomerular lesion leads to proteinuria, which may be heavy. Renal hemodynamic changes include modest decreases in the glomerular filtration rate (GFR) and renal blood flow (RBF). Decreased sodium and uric acid excretion may be caused by increased proximal tubular reabsorption. The mechanism for the marked hypocalciuria is not known.
Kidney Disease and Hypertension in Pregnancy

Trial Number of trials Antplatelet therapy Control therapy Odds ratio and 95% CI (horizontal line) (antiplatelet; placebo)

Smaller studies (<200 women) 11 10/319 (3.1%) 50/284 (17.6%)

Larger studies:
- EPHREDA (1990)
- Hauth (1993)
- Italian (1993)
- Sibai (1993)
- Viinikka (1993)
- CLASP (1994)

All larger trials

All trials 17 423/7675 (5.5%) 542/7458 (7.3%)

FIGURE 10-35
Prevention of preeclampsia with low-dose aspirin. Investigators have sought methods to prevent preeclampsia (eg, salt restriction, prophylactic diuretics, and high-protein diets). One approach that has been extensively investigated in the last 10 years is therapy with low-dose aspirin. It was hypothesized that such therapy reversed the imbalance between prostacyclin and thromboxane that may be responsible for some of the manifestations of the disease. Several large trials now have been completed, and most have had negative results. Shown here is an overview of the effects of aspirin on proteinuric preeclampsia reported from all trials of antiplatelet therapy (through 1994) as analyzed by the Collaborative Low-dose Aspirin in Pregnancy (CLASP) Collaborative Group [28]. Odds ratios (area proportional to amount of information contributed) and 99% confidence interval (CI) are plotted for various trials. A black square to the left of the solid vertical line suggests a benefit (however, this indication is significant at 2p >0.01 only if the entire CI is to the left of solid vertical line). (From CLASP Collaborative Group [29]; with permission.)

FIGURE 10-36
Prevention of preeclampsia using calcium supplementation. Another preventive strategy that has been extensively investigated, with conflicting outcomes, is calcium supplementation. The rationale for this approach is based on the observations that low dietary calcium intake may increase the risk for preeclampsia, and that preeclampsia is characterized by abnormalities in calcium metabolism that suggest a calcium deficit, eg, decreased vitamin D and hypocalciuria [31]. A recent meta-analysis of 14 trials of calcium supplementation in pregnancy concluded that calcium supplementation during pregnancy leads to reductions in blood pressure and a lower incidence of preeclampsia. In contrast, a large randomized trial of calcium supplementation in 4589 low-risk women failed to demonstrate a benefit of calcium therapy [31]. CI—confidence interval; OR—odds ratio. (From Bucher and coworkers [30]; with permission.)
**TREATMENT OF PREECLAMPSIA**

- Close monitoring of maternal and fetal conditions
- Hospitalization in most cases
- Lower blood pressure for maternal safety
- Seizure prophylaxis with magnesium sulfate
- Timely delivery

**ANTIHYPERTENSIVE THERAPY IN PREECLAMPSIA**

Decreased uteroplacental blood flow and placental ischemia are central to the pathogenesis of preeclampsia. Lowering blood pressure does not prevent or cure preeclampsia and does not benefit the fetus unless delivery can be safely postponed.

Lowering blood pressure is appropriate for maternal safety: maintain blood pressure at 130–150/85–100 mm Hg.

**FIGURE 10-37**

Treatment of preeclampsia requires close monitoring of both the maternal and fetal condition to maximize chances of avoiding catastrophes such as seizures, renal failure, and fetal demise. Close surveillance is best accomplished in the hospital in all but the mildest cases. Maternal hypertension should be treated to avoid cerebrovascular and cardiovascular complications. Magnesium sulfate is the treatment of choice for seizure prophylaxis and usually is instituted immediately after delivery. When the fetus is mature, delivery is indicated in all cases. When the fetus is immature, the decision to deliver is made after carefully assessing both the maternal and fetal condition. When maternal health is in jeopardy, delivery is necessary, even with a premature fetus.

**FIGURE 10-38**

Some controversy exists regarding when to institute antihypertensive therapy in women with preeclampsia. The basis for this controversy is that decreased uteroplacental perfusion is believed to be important in the pathophysiology of this disorder, and concern exists that lowering maternal blood pressure may compromise uteroplacental blood flow and lead to fetal distress. Furthermore, lowering maternal blood pressure does not cure preeclampsia. Thus, antihypertensive therapy is instituted when the blood pressure reaches a level at which the physician considers the maternal condition to be in danger from hypertension. For most physicians, this treatment threshold is at approximately 150/100 mm Hg. Aggressive lowering of blood pressure is not advisable.

**FIGURE 10-39**

When blood pressure increases acutely and delivery is likely within the next 24 hours, use of a parenteral antihypertensive agent is preferable. Intravenous hydralazine or labetalol are acceptable agents for pregnant women, and both have been used successfully in preeclampsia. Calcium channel blockers should be used with caution because they may act synergistically with magnesium sulfate, resulting in precipitous decreases in blood pressure. Rarely, agents such as diazoxide may be needed; however, when hypertension is severe, maternal safety takes priority over pregnancy status. When delivery can be postponed safely for several days, an oral agent is indicated. Methyldopa is one of the safest drugs in pregnancy and has been used extensively with excellent maternal and fetal outcome. Labetalol and other β blockers have been used successfully in preeclampsia. Calcium channel blockers also may be used as either second- or third-line agents. Oral hydralazine is safe in pregnancy. Limited experience exists with α blockers or clonidine, although anecdotal reports suggest these agents are safe.