much higher than that required for these functions. The major function of autoregulation in the kidneys is to maintain a relatively constant GFR and to allow precise control of renal excretion of water and solutes.

The GFR normally remains autoregulated (that is, remains relatively constant), despite considerable arterial pressure fluctuations that occur during a person's usual activities. For instance, a decrease in arterial pressure to as low as 75 mm Hg or an increase to as high as 160 mm Hg usually changes GFR less than 10%. In general, renal blood flow is autoregulated in parallel with GFR, but GFR is more efficiently autoregulated under certain conditions.

Myogenic Autoregulation of Renal Blood Flow and GFR

Another mechanism that contributes to the maintenance of a relatively constant renal blood flow and GFR is the ability of individual blood vessels to resist stretching during increased arterial pressure, a phenomenon referred to as the *myogenic mechanism*. Studies of individual blood vessels (especially small arterioles) throughout the body have shown that they respond to increased wall tension or wall stretch by contraction of the vascular smooth muscle. Stretch of the vascular wall allows increased movement of calcium ions from the extracellular fluid into the vascular smooth muscle cells causing them to contract by combining with intracellular calmodulin and the activation of myosin cross bridges. This contraction prevents excessive stretch of the vessel and at the same time, by raising vascular resistance, helps prevent excessive increases in renal blood flow and GFR when arterial pressure increases.

Although the myogenic mechanism probably operates in most arterioles throughout the body, its importance in renal blood flow and GFR autoregulation has been questioned by some physiologists because this pressure-sensitive mechanism has no means of directly detecting changes in renal blood flow or GFR per se. On the other hand, this mechanism may be more important in protecting the kidney from hypertension-induced injury. In response to sudden increases in blood pressure, the myogenic constrictor response in afferent arterioles occurs within seconds and therefore attenuates transmission of increased arterial pressure to the glomerular capillaries.

Glomerular Filtration—The First Step in Urine Formation

Composition of the Glomerular Filtrate

Urine formation begins with filtration of large amounts of fluid through the glomerular capillaries into Bowman's capsule. Like most capillaries, the glomerular capillaries are relatively impermeable to proteins, so the filtered fluid (called the *glomerular filtrate*) is essentially protein free and devoid of cellular elements, including red blood cells.

The concentrations of other constituents of the glomerular filtrate, including most salts and organic molecules, are similar to the concentrations in the plasma. Exceptions to this generalization include a few low-molecular-weight substances, such as calcium and fatty acids, that are not freely filtered because they are partially bound to the plasma proteins.

GFR Is About Twenty Percent of the Renal Plasma Flow

As in other capillaries, the GFR is determined by (1) the balance of hydrostatic and colloid osmotic forces acting across the capillary membrane and (2) the capillary filtration coefficient (K_f), the product of the permeability and filtering surface area of the capillaries. The glomerular capillaries have a much higher rate of filtration than most other capillaries because of a high glomerular hydrostatic pressure and a large K_f. In the average adult human, the GFR is about 125 ml/min or 180 L/day. The fraction of the renal plasma flow that is filtered (the filtration fraction) averages about 0.2; this means that about 20% of the plasma flowing through the kidney is filtered through the glomerular capillaries. The filtration fraction is calculated as follows:

Filtration fraction = GFR/Renal plasma flow

Glomerular Capillary Membrane

The glomerular capillary membrane is simila to that of other capillaries, except that it has three (ins ad of the usual two) major layers: (1) the *endothelium* of t capillary, (2) a *basement membrane*, and (3) a layer of *epi lial cells* (*podocytes*) surrounding the outer surface of tl capillary basement membrane (Figure 77-5). Together, t e layers make up the filtration barrier, which, despite the ree layers, filters several hundred times as much water a solutes as the usual capillary membrane. Even with this gh rate of filtration, the glomerular capillary membrane rmally prevents filtration of plasma proteins.

The high filtration rate across the glomerular pillary membrane is due partly to its special characteris s. The capillary *endothelium* is perforated by thousands small holes called *fenestrae*, similar to the fenestrated c llaries found in the liver. Although the fenestrations are atively large, endothelial cells are richly endowed with fix nega- tive charges that hinder the passage of plasma prot is.

Surrounding the endothelium is the *basemen mem- brane*, which consists of a meshwork of collagen a l pro- teoglycan fibrillae that have large spaces throug which large amounts of water and small solutes can filter. The basement membrane effectively prevents filtration of plasma proteins, in part because of strong negative electrical charges associated with the proteoglycans.

The final part of the glomerular membrane is a layer of epithelial cells that line the outer surface of the glomerulus. These cells are not continuous but have long foot-like

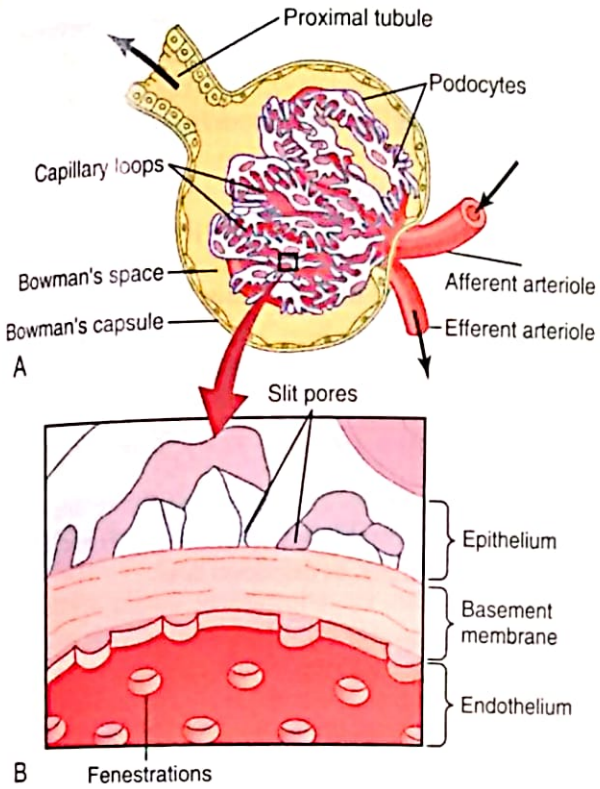

Figure 77-5 *A*, Basic ultrastructure of the glomerular capillaries. *B*, Cross section of the glomerular capillary membrane and its major components: capillary endothelium, basement membrane, and epithelium (podocytes).

processes (podocytes) that encircle the outer surface of the capillaries (see Figure 77-5). The foot processes are separated by gaps called *slit pores* through which the glomerular filtrate moves. The epithelial cells, which also have negative charges, provide additional restriction to filtration of plasma proteins. Thus, all layers of the glomerular capillary wall provide a barrier to filtration of plasma proteins.

Filterability of Solutes Is Inversely Related to Their Size. The glomerular capillary membrane is thicker than most other capillaries, but it is also much more porous and therefore filters fluid at a high rate. Despite the high filtration rate, the glomerular filtration barrier is selective in determining which molecules will filter, based on their size and electrical charge.

Table 77-2 lists the effect of molecular size on filterability of different molecules. A filterability of 1.0 means that the substance is filtered as freely as water; a filterability of 0.75 means that the substance is filtered only 75% as rapidly as water. Note that electrolytes such as sodium and small organic compounds such as glucose are freely filtered. As the molecular weight of the molecule approaches that of albumin, the filterability rapidly decreases, approaching zero.

Negatively Charged Large Molecules Are Filtered Less Easily Than Positively Charged Molecules of Equal Molecular Size. The molecular diameter of the plasma protein albumin is only about 6 nanometers, whereas the pores of the glomerular membrane are thought to be about 8 nanometers (80 angstroms). Albumin is restricted from

Table 77-2 Filterability of Substances by Glomerular Capillaries Based on Molecular Weight

Substance	Molecular Weight	Filterability
Water	18	1
Sodium	23	1
Glucose	180	1
Inulin	5500	1
Myoglobin	17,000	0.75
Albumin	69,000	0.005

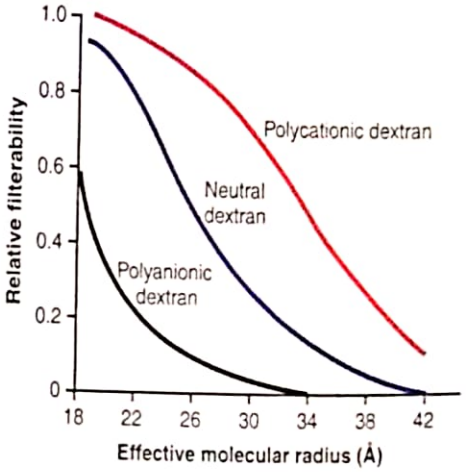

Figure 77-6 Effect of molecular radius and electrical charge of dextran on its filterability by the glomerular capillaries. A value of 1.0 indicates that the substance is filtered as freely as water, whereas a value of 0 indicates that it is not filtered. Dextrans are polysaccharides that can be manufactured as neutral molecules or with negative or positive charges and with varying molecular weights.

filtration, however, because of its negative charge and the electrostatic repulsion exerted by negative charges of the glomerular capillary wall proteoglycans.

Figure 77-6 shows how electrical charge affects the filtration of different molecular weight dextrans by the glomerulus. Dextrans are polysaccharides that can be manufactured as neutral molecules or with negative or positive charges. Note that for any given molecular radius, positively charged molecules are filtered much more readily than negatively charged molecules. Neutral dextrans are also filtered more readily than negatively charged dextrans of equal molecular weight. The reason for these differences in filterability is that the negative charges of the basement membrane and the podocytes provide an important means for restricting large negatively charged molecules, including the plasma proteins.

In certain kidney diseases, the negative charges on the basement membrane are lost even before there are noticeable changes in kidney histology, a condition referred to as *minimal change nephropathy*. As a result of this loss of negative charges on the basement membranes some of the lower-molecular-weight proteins, especially albumin, are filtered and appear in the urine, a condition known as *proteinuria* or *albuminuria*.

Determinants of the GFR

See Appendix for a detailed description of the measurement of GFR by the renal clearance of inulin and creatinine.

The GFR is determined by (1) the sum of the hydrostatic and colloid osmotic forces across the glomerular membrane, which gives the *net filtration pressure*, and (2) the glomerular capillary filtration coefficient, K_f. Expressed mathematically, the GFR equals the product of K_f and the net filtration pressure:

$$\text{GFR} = K_f \times \text{Net filtration pressure}$$

The net filtration pressure represents the sum of the hydrostatic and colloid osmotic forces that either favor or oppose filtration across the glomerular capillaries (Figure 77-7). These forces include (1) hydrostatic pressure inside the glomerular capillaries (glomerular hydrostatic pressure, P_G), which promotes filtration; (2) the hydrostatic pressure in Bowman's capsule (P_B) outside the capillaries, which opposes filtration; (3) the colloid osmotic pressure of the glomerular capillary plasma proteins (π_G), which opposes filtration; and (4) the colloid osmotic pressure of the proteins in Bowman's capsule (π_B), which promotes filtration. (Under normal conditions, the concentration of protein in the glomerular filtrate is so low that the colloid osmotic pressure of the Bowman's capsule fluid is considered to be zero.)

The GFR can therefore be expressed as:

$$\text{GFR} = K_f \times (P_G - P_B - \pi_G + \pi_B)$$

Although the normal values for the determinants of GFR have not been measured directly in humans, they have been estimated in animals such as dogs and rats. Based on the results in animals, the approximate normal forces favoring and opposing glomerular filtration in humans are believed to be as follows (see Figure 77-7):

Forces Favoring Filtration (mm Hg)

Glomerular hydrostatic pressure	60
Bowman's capsule colloid osmotic pressure	0

Forces Opposing Filtration (mm Hg)

Bowman's capsule hydrostatic pressure	18
Glomerular capillary colloid osmotic pressure	32

$$\text{Net filtration} = 60 - 18 - 32 = +10 \text{ mm Hg}$$

Some of these values can change markedly under different physiologic conditions, whereas others are altered mainly in disease states, as discussed later.

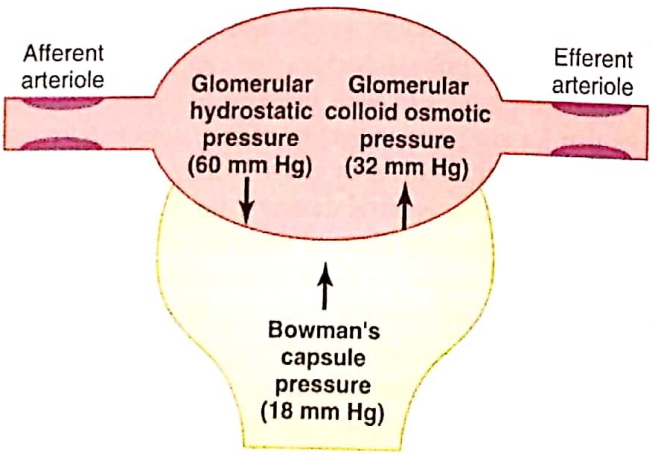

Figure 77-7 Summary of forces causing filtration by the glomerular capillaries. The values shown are estimates for healthy humans.

Increased Glomerular Capillary Filtration Coefficient Increases GFR

The K_f is a measure of the product of the hydraulic conductivity and surface area of the glomerular capillaries. The K_f cannot be measured directly, but it is estimated experimentally by dividing the rate of glomerular filtration by net filtration pressure:

$$K_f = \text{GFR}/\text{Net filtration pressure}$$

Because total GFR for both kidneys is about 125 ml/min and the net filtration pressure is 10 mm Hg, the normal K_f is calculated to be about 12.5 ml/min/mm Hg of filtration pressure. Although increased K_f raises GFR and decreased K_f reduces GFR, changes in K_f probably do not provide a primary mechanism for the normal day-to-day regulation of GFR. Some diseases, however, lower K_f by reducing the number of functional glomerular capillaries (the by reducing the surface area for filtration) or by increasing the thickness of the glomerular capillary membrane and reducing its hydraulic conductivity. For example, chronic, uncontrolled hypertension and diabetes mellitus gradually reduce K_f by increasing the thickness of the glomerular capillary basement membrane and, eventually, by damaging capillaries so severely that there is loss of capillary function.

Increased Bowman's Capsule Hydrostatic Pressure Decreases GFR

Direct measurements, using micropipettes, of hydrostatic pressure in Bowman's capsule and at different points in the proximal tubule in experimental animals suggest that a reasonable estimate for Bowman's capsule pressure in humans is about 18 mm Hg under normal conditions. Increasing the hydrostatic pressure in Bowman's capsule reduces GFR, whereas decreasing this pressure raises GFR. However, changes in Bowman's capsule pressure normally do not serve as a primary means for regulating GFR.

In certain pathological states associated with obstruction of the [illegible] pressure can

increase markedly, causing serious reduction of GFR. For example, precipitation of calcium or of uric acid may lead to "stones" that lodge in the urinary tract, often in the ureter, thereby obstructing outflow of the urinary tract and raising Bowman's capsule pressure. This reduces GFR and eventually can cause *hydronephrosis* (distention and dilation of the renal pelvis and calyces) and can damage or even destroy the kidney unless the obstruction is relieved.

Increased Glomerular Capillary Colloid Osmotic Pressure Decreases GFR

As blood passes from the afferent arteriole through the glomerular capillaries to the efferent arterioles, the plasma protein concentration increases about 20% (Figure 77-8). The reason for this is that about one-fifth of the fluid in the capillaries filters into Bowman's capsule, thereby concentrating the glomerular plasma proteins that are not filtered. Assuming that the normal colloid osmotic pressure of plasma entering the glomerular capillaries is 28 mm Hg, this value usually rises to about 36 mm Hg by the time the blood reaches the efferent end of the capillaries. Therefore, the average colloid osmotic pressure of the glomerular capillary plasma proteins is midway between 28 and 36 mm Hg, or about 32 mm Hg.

Thus, two factors that influence the glomerular capillary colloid osmotic pressure are (1) the arterial plasma colloid osmotic pressure and (2) the fraction of plasma filtered by the glomerular capillaries (filtration fraction). Increasing the arterial plasma colloid osmotic pressure raises the glomerular capillary colloid osmotic pressure, which in turn decreases GFR.

Increased Glomerular Capillary Hydrostatic Pressure Increases GFR

The glomerular capillary hydrostatic pressure has been estimated to be about 60 mm Hg under normal conditions. Changes in glomerular hydrostatic pressure serve as the primary means for physiologic regulation of GFR. Increases in glomerular hydrostatic pressure raise GFR, whereas decreases in glomerular hydrostatic pressure reduce GFR.

Glomerular hydrostatic pressure is determined by three variables, each of which is under physiologic control: (1) *arterial pressure*, (2) *afferent arteriolar resistance*, and (3) *efferent arteriolar resistance*.

Increased arterial pressure tends to raise glomerular hydrostatic pressure and, therefore, to increase GFR. (However, as discussed later, this effect is buffered by autoregulatory mechanisms that maintain a relatively constant glomerular pressure as blood pressure fluctuates.)

Increased resistance of afferent arterioles reduces glomerular hydrostatic pressure and decreases GFR. Conversely, dilation of the afferent arterioles increases both glomerular hydrostatic pressure and GFR (Figure 77-9).

Constriction of the efferent arterioles increases the resistance to outflow from the glomerular capillaries. This raises the glomerular hydrostatic pressure, and as long as the increase in efferent resistance does not reduce renal blood flow too much, GFR increases slightly (see Figure 77-9). Table 77-3 summarizes the factors that can decrease GFR.

Physiologic Control of Glomerular Filtration and Renal Blood Flow

The determinants of GFR that are most variable and subject to physiologic control include the glomerular hydrostatic pressure and the glomerular capillary colloid osmotic pressure.

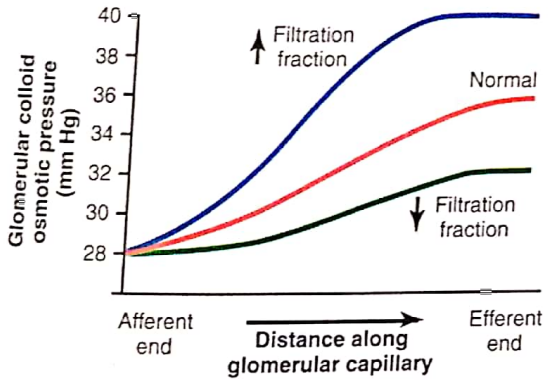

Figure 77-8 Increase in colloid osmotic pressure in plasma flowing through the glomerular capillary. Normally, about one-fifth of the fluid in the glomerular capillaries filters into Bowman's capsule, thereby concentrating the plasma proteins that are not filtered. Increase in the filtration fraction (glomerular filtration rate/renal plasma flow) increases the rate at which the plasma colloid osmotic pressure rises along the glomerular capillary; decrease in the filtration fraction has the opposite effect.

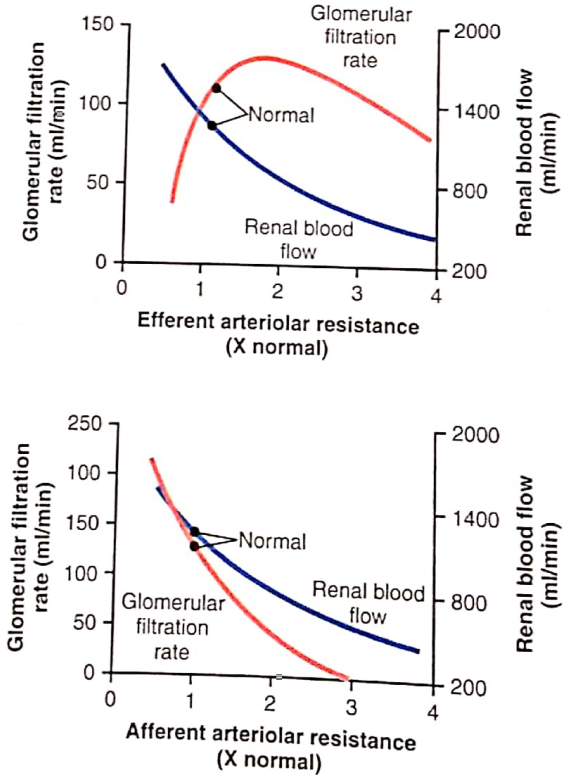

Figure 77-9 Effect of change in afferent arteriolar resistance or efferent arteriolar resistance on glomerular filtration rate and renal blood flow.

Table 77-3 Factors That Can Decrease the Glomerular Filtration Rate (GFR)

Physical Determinants*	Physiologic/Pathophysiologic Causes
↓ K_f→↓ GFR	Renal disease, diabetes mellitus, hypertension
↑ P_B→↓ GFR	Urinary tract obstruction (e.g., kidney stones)
↑ π_G→↓ GFR	↓ Renal blood flow, increased plasma proteins
↓ P_G→↓ GFR ↓ A_P→↓ P_G	↓ Arterial pressure (has only small effect due to autoregulation)
↓ R_E→↓ P_G	↓ Angiotensin II (drugs that block angiotensin II formation)
↑ R_A→↓ P_G	↑ Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)

*Opposite changes in the determinants usually increase GFR.
K_f, glomerular filtration coefficient; P_B, Bowman's capsule hydrostatic pressure; π_G, glomerular capillary colloid osmotic pressure; P_G, glomerular capillary hydrostatic pressure; A_P, systemic arterial pressure; R_E, efferent arteriolar resistance; R_A, afferent arteriolar resistance.

These variables, in turn, are influenced by the sympathetic nervous system, hormones and autacoids (vasoactive substances that are released in the kidneys and act locally), and other feedback controls that are intrinsic to the kidneys.

Sympathetic Nervous System Activation Decreases GFR

Essentially all the blood vessels of the kidneys, including the afferent and the efferent arterioles, are richly innervated by sympathetic nerve fibers. Strong activation of the renal sympathetic nerves can constrict the renal arterioles and decrease renal blood flow and GFR. Moderate or mild sympathetic stimulation has little influence on renal blood flow and GFR. For example, reflex activation of the sympathetic nervous system resulting from moderate decreases in pressure at the carotid sinus baroreceptors or cardiopulmonary receptors has little influence on renal blood flow or GFR.

The renal sympathetic nerves seem to be most important in reducing GFR during severe, acute disturbances lasting for a few minutes to a few hours, such as those elicited by the defense reaction, brain ischemia, or severe hemorrhage. In the healthy resting person, sympathetic tone appears to have little influence on renal blood flow.

Hormonal and Autacoid Control of Renal Circulation

Several hormones and autacoids can influence GFR and renal blood flow, as summarized in Table 77-4.

Norepinephrine, Epinephrine, and Endothelin Constrict Renal Blood Vessels and Decrease GFR. Hormones that constrict afferent and efferent arterioles, causing reductions in GFR and renal blood flow, include *norepinephrine* and *epinephrine* released from the adrenal medulla. In general, blood levels of these hormones parallel the activity of the sympathetic nervous system; thus, norepinephrine and epinephrine have little influence on renal hemodynamics except under extreme conditions, such as severe hemorrhage.

Table 77-4 Hormones and Autacoids That Influence Glomerular Filtration Rate (GFR)

Hormone or Autacoid	Effect on GFR
Norepinephrine	↓
Epinephrine	↓
Endothelin	↓
Angiotensin II	– (prevents ↓)
Endothelial-derived nitric oxide	↑
Prostaglandins	↑

Another vasoconstrictor, *endothelin*, is a peptide that can be released by damaged vascular endothelial cells of the kidneys, as well as by other tissues. The physiologic role of this autacoid is not completely understood. However, endothelin may contribute to hemostasis (minimizing blood loss) when a blood vessel is severed, which damages the endothelium and releases this powerful vasoconstrictor.

Angiotensin II Preferentially Constricts Efferent Arterioles in Most Physiologic Conditions. A powerful renal vasoconstrictor, *angiotensin II*, can be considered a circulating hormone as well as a locally produced autacoid because it is formed in the kidneys and in the systemic circulation. Receptors for angiotensin II are present in virtually all blood vessels of the kidneys. However, the preglomerular blood vessels, especially the afferent arterioles, appear to be relatively protected from angiotensin II-mediated constriction in most physiologic conditions associated with activation of the renin–angiotensin system such as during a low-sodium diet or reduced renal perfusion pressure due to renal artery stenosis. This protection is due to release of vasodilators, especially *nitric oxide* and *prostaglandins*, which counteract the vasoconstrictor effects of angiotensin II in these blood vessels.

The efferent arterioles, however, are highly sensitive to angiotensin II. Because angiotensin II preferentially constricts efferent arterioles in most physiologic conditions, increased angiotensin II levels raise glomerular hydrostatic pressure while reducing renal blood flow. It should be kept in mind that increased angiotensin II formation usually occurs in circumstances associated with decreased arterial pressure or volume depletion, which tend to decrease GFR. In these circumstances, the increased level of angiotensin II, by constricting efferent arterioles, helps *maintain* glomerular hydrostatic pressure and GFR; at the same time, though, the reduction in renal blood flow caused by efferent arteriolar constriction contributes to decreased flow through the

peritubular capillaries, which in turn increases reabsorption of sodium and water, as discussed in Chapter 78.

Endothelial-Derived Nitric Oxide Decreases Renal Vascular Resistance and Increases GFR. An autacoid that decreases renal vascular resistance and is released by the vascular endothelium throughout the body is *endothelial-derived nitric oxide*. A basal level of nitric oxide production appears to be important for maintaining vasodilation of the kidneys. This allows the kidneys to excrete normal amounts of sodium and water. Therefore, administration of drugs that inhibit formation of nitric oxide increases renal vascular resistance and decreases GFR and urinary sodium excretion, eventually causing high blood pressure. In some hypertensive patients or in patients with atherosclerosis, damage of the vascular endothelium and impaired nitric oxide production may contribute to increased renal vasoconstriction and elevated blood pressure.

Prostaglandins and Bradykinin Tend to Increase GFR. Hormones and autacoids that cause vasodilation and increased renal blood flow and GFR include the prostaglandins (PGE_2 and PGI_2) and bradykinin. These substances are discussed in Chapter 45. Although these vasodilators do not appear to be of major importance in regulating renal blood flow or GFR in normal conditions, they may dampen the renal vasoconstrictor effects of the sympathetic nerves or angiotensin II, especially their effects to constrict the afferent arterioles.

By opposing vasoconstriction of afferent arterioles, the prostaglandins may help prevent excessive reductions in GFR and renal blood flow. Under stressful conditions, such as volume depletion or after surgery, the administration of nonsteroidal anti-inflammatory agents, such as aspirin, that inhibit prostaglandin synthesis may cause significant reductions in GFR.

Tubuloglomerular Feedback and Autoregulation of GFR

To perform the function of autoregulation, the kidneys have a feedback mechanism that links changes in sodium chloride concentration at the macula densa with the control of renal arteriolar resistance. This feedback helps ensure a relatively constant delivery of sodium chloride to the distal tubule and helps prevent spurious fluctuations in renal excretion that would otherwise occur. In many circumstances, this feedback autoregulates renal blood flow and GFR in parallel. However, because this mechanism is specifically directed toward stabilizing sodium chloride delivery to the distal tubule, there are instances when GFR is autoregulated at the expense of changes in renal blood flow, as discussed later.

The tubuloglomerular feedback mechanism has two components that act together to control GFR: (1) an afferent arteriolar feedback mechanism and (2) an efferent arteriolar feedback mechanism. These feedback mechanisms depend on special anatomical arrangements of the *juxtaglomerular complex* (Figure 77-10).

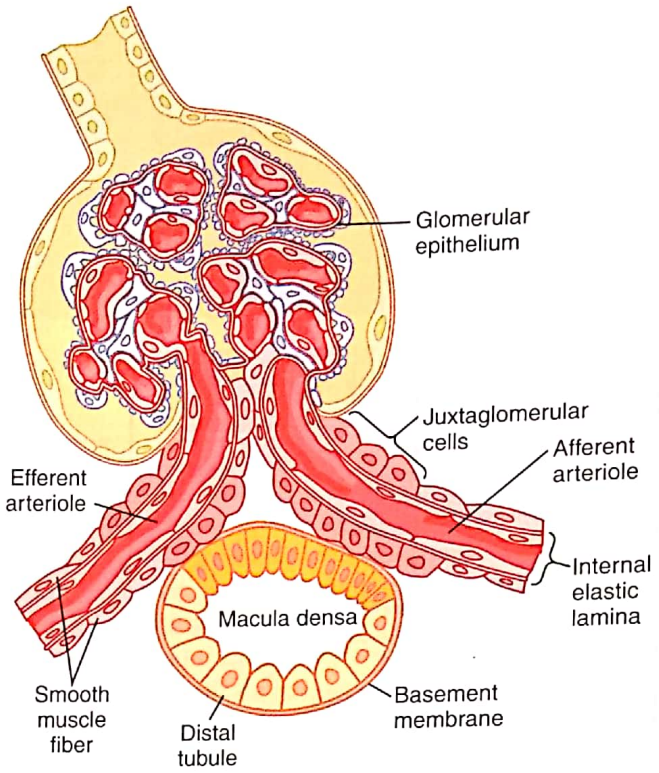

Figure 77-10 Structure of the juxtaglomerular apparatus, demonstrating its possible feedback role in the control of nephron function.

The juxtaglomerular complex consists of *macula densa cells* in the initial portion of the distal tubule and *juxtaglomerular cells* in the walls of the afferent and efferent arterioles. The macula densa is a specialized group of epithelial cells in the distal tubules that comes in close contact with the afferent and efferent arterioles. The macula densa cells contain Golgi apparatus, which are intracellular secretory organelles directed toward the arterioles, suggesting that these cells may be secreting a substance toward the arterioles.

Decreased Macula Densa Sodium Chloride Causes Dilation of Afferent Arterioles and Increased Renin Release. The macula densa cells sense changes in volume delivery to the distal tubule by way of signals that are not completely understood. Experimental studies suggest that decreased GFR slows the flow rate in the loop of Henle, causing increased reabsorption of sodium and chloride ions in the ascending loop of Henle, thereby reducing the concentration of sodium chloride at the macula densa cells. This decrease in sodium chloride concentration initiates a signal from the macula densa that has two effects (Figure 77-11): (1) It decreases resistance to blood flow in the afferent arterioles, which raises glomerular hydrostatic pressure and helps return GFR toward normal, and (2) it increases renin release from the juxtaglomerular cells of the afferent and efferent arterioles, which are the major storage sites for renin. Renin released from these cells then functions as an enzyme to increase the formation of angiotensin I, which is converted to angiotensin II. Finally, the angiotensin II constricts the

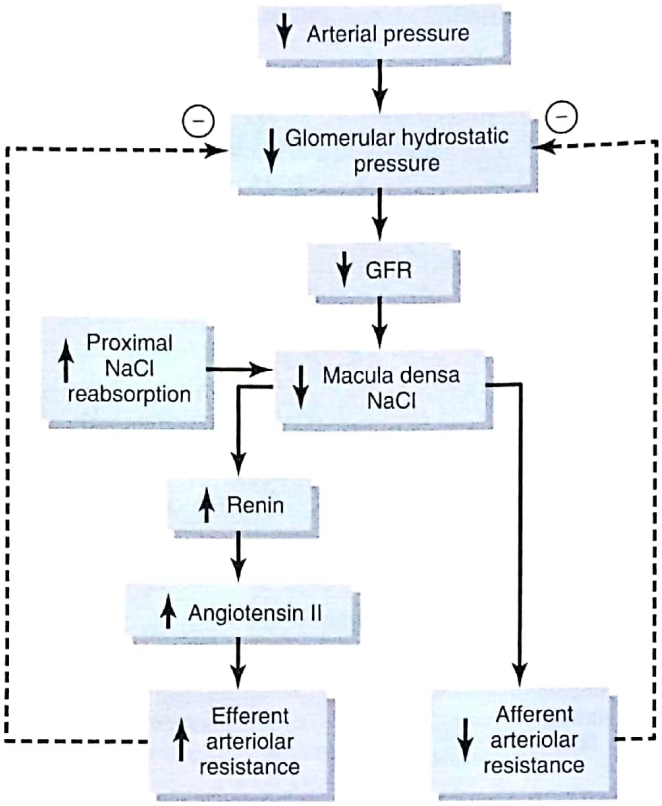

Figure 77-11 Macula densa feedback mechanism for autoregulation of glomerular hydrostatic pressure and glomerular filtration rate (GFR) during decreased renal arterial pressure.

efferent arterioles, thereby increasing glomerular hydrostatic pressure and helping to return GFR toward normal.

Other Factors That Increase Renal Blood Flow and GFR: High Protein Intake and Increased Blood Glucose. Although renal blood flow and GFR are relatively stable under most conditions, there are circumstances in which these variables change significantly. For example, *a high protein intake is known to increase both renal blood flow and GFR.* With a chronic high-protein diet, such as one that contains large amounts of meat, the increases in GFR and renal blood flow are due partly to growth of the kidneys. However, GFR and renal blood flow increase 20 to 30% within 1 or 2 hours after a person eats a high-protein meal.

A similar mechanism may also explain the marked increases in renal blood flow and GFR that occur with large increases in blood glucose levels in uncontrolled diabetes mellitus. Because glucose, like some of the amino acids, is also reabsorbed along with sodium in the proximal tubule, increased glucose delivery to the tubules causes them to reabsorb excess sodium along with glucose. This, in turn, decreases delivery of sodium chloride to the macula densa, activating a tubuloglomerular feedback-mediated dilation of the afferent arterioles and subsequent increases in renal blood flow and GFR.

These examples demonstrate that renal blood flow and GFR per se are not the primary variables controlled by the tubuloglomerular feedback mechanism. The main purpose of this feedback is to ensure a constant delivery of sodium chloride to the distal tubule, where final processing of the urine takes place. Thus, disturbances that tend to increase reabsorption of sodium chloride at tubular sites before the macula densa tend to elicit increased renal blood flow and GFR, which helps return distal sodium chloride delivery towards normal so that normal rates of sodium and water excretion can be maintained (see Figure 77-11).

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