Cardiovascular manifestations are a frequent finding in hyperthyroidism and hypothyroidism. It has been debated whether these alterations are the consequence solely of increased cardiac work load or an intrinsic property of thyroid hormones. Today, there is clear evidence for direct effects of these hormones on the myocardium in addition to indirect ones. In this review, we focus on the cardiovascular manifestations of thyroid dysfunction. We first briefly discuss the three potential mechanisms by which thyroid hormones might exert their cardiovascular actions: 1) by direct effects at the cellular level, 2) by interacting with the sympathetic nervous system, and 3) through alterations of the peripheral circulation and energy metabolism. Then, the consequences of such thyroid hormone effects on some particular aspects of cardiovascular function are examined. Finally, the mechanisms that may lead to the rare event of heart failure in patients with thyroid disease in the absence of preexisting heart disease are evoked.

**Direct Effects of Thyroid Hormones at the Cellular Level**

The active thyroid hormone T₃ exerts its effects mainly at the cellular level through activation of mRNA coding for specific proteins via binding to specific nuclear receptors.⁠¹ These nuclear receptors belong to the c-erbA superfamilly.⁠¹ So far, four receptors have been described. Three of them — α₁, β₁, and β₂-receptors — have a high binding affinity for T₃, whereas the α₂-receptor has no T₃-binding domain and is likely to function as a T₃ antagonist. In the rat, the three T₃-binding receptors have a specific tissue distribution. The α-receptors are ubiquitous in all tissues. The β-receptors appear to be regulated by various expression factors, including thyroid hormones, and are expressed in thyroid hormone-responsive tissues such as liver, kidney, brain, and heart. The β₂-receptor is particular because it is expressed only in the pituitary and hypothalamus.⁠¹² It is likely that the distribution of these receptors in humans is similar, if not identical, to that found in the rat, even though the human β₂-receptor has not been cloned.

The effects of T₃ are complex and multiple, some being stimulant, others inhibitory, and many of them occurring in concert with other hormones and factors. In the myocardium of some animal species, T₃ can change the spectrum of myosin heavy chain and Na⁺,K⁺-ATPase isoforms; in the human, it may act mainly by stimulating the sarcoplasmic calcium ATPase, an enzyme that is involved in diastolic relaxation. Other well-known determinants of cardiac function, ANP and the cytosolic malic enzyme, also are partly controlled by T₃.⁠³⁴ Apart from their nuclear receptor-mediated effect, thyroid hormones also have been shown to activate extranuclear sites. This concept is based on the observation that T₃ increases cellular amino acid and sugar uptake in the presence of a protein-synthesis inhibitor.⁠⁵⁶ However, these observations and their physiological relevance remain controversial.⁠² Finally, T₃ also may alter plasma membrane function. Segal⁷ has reported facilitation of rapid calcium uptake by rat heart slices after addition of physiological concentration of T₃ to the media. This effect was directly proportional to T₃ concentration, thyroid hormone specific, and independent of extracellular calcium concentration. This suggests a rapid plasma membrane-mediated action of thyroid hormones with calcium as the second messenger.⁷

**Interaction of Thyroid Hormones With the Sympathetic Nervous System**

Many clinical manifestations of hyperthyroidism, such as tremor, tachycardia, eyelid retraction, and anxiety, mimic a hyperadrenergic state, whereas clinical manifestations of hypothyroidism such as sinus bradycardia are suggestive of decreased sympathetic tone.⁶ However, these clinical findings suggestive of an altered sympathetic tone are not reflected by circulating plasma catecholamine concentrations, which are normal or decreased in hyperthyroidism and elevated in hypothyroidism.⁴⁻¹¹ The latter finding is not related to decreased norepinephrine clearance but rather to increased norepinephrine release from sympathetic nerves.⁹¹¹ This interpretation is strengthened by the observation that thyrotropin releasing hormone (TRH), which is elevated in primary hypothyroidism, directly stimulates sympathetic outflow within the central nervous system and may be taken up by nerve endings to serve as a neurotransmitter.¹³⁻¹⁶ This apparent paradox of clinical signs evoking decreased sympathetic tone in the presence of elevated norepinephrine release from sympathetic nerve endings is consistent with the hypothesis of a desensitization to the effects of catecholamines in hypothyroidism. On the other hand, the hyperadrenergic state seen in hyperthyroidism suggests hypersensitivity to catecholamines.

The mechanism by which thyroid hormones might alter the responsiveness to catecholamines is still unknown.¹⁷ In some studies, hyperthyroidism has been found to be associated with increased receptor density, whereas the reverse is true for hypothyroidism.¹⁸⁻²¹ In
In this regard, Insel\textsuperscript{12} recently reported that thyroid hormones might regulate $\beta$-adrenergic receptor density by modulating receptor formation rate, degradation rate, or both. Data regarding effects of thyroid hormones on stimulation of adenylate cyclase activity by isoproterenol administration are conflicting.\textsuperscript{18,19,23} Hyperthyroid pigs show increased responsiveness to $\beta$ stimulation,\textsuperscript{20} a finding that may be related to increased $G_\text{i}$ density in myocardial membranes.\textsuperscript{19} Differences between studies may be related to the model used. For example, adrenergic receptor modulation induced by short-term administration of $T_3$ may differ from that found in clinical hyperthyroidism. Results obtained from in vitro studies of adrenergic receptors isolated from peripheral tissues such as leukocytes or adipocytes may not apply to myocardial adrenergic receptors because differences in sympathetic innervation may greatly alter adenylate cyclase activity.\textsuperscript{24}

Few studies have been performed in humans to test the effects of thyroid state on responsiveness to adrenergic stimulation. A study by Martin et al\textsuperscript{25} has shown that short-term hyperthyroidism is associated with an increase of the sensitivity of heart rate and left ventricular shortening velocity to isoproterenol stimulation. Hyperthyroid patients display augmented heart rate and systolic blood pressure responses to exogenously administered catecholamines, a finding that had been used as a diagnostic test before thyroid hormone assays became available, as reported by Levey et al.\textsuperscript{17} In hypothyroid patients, some studies found evidence for decrease of $\alpha$- and $\beta$-adrenergic sensitivity.\textsuperscript{26,27} The clinical observation in myxedematous patients of hemodynamic shock resistant to catecholamine administration is consistent with this hypothesis.\textsuperscript{28} However, other studies found no evidence for decreased $\beta$-adrenergic sensitivity in hypothyroid patients.\textsuperscript{29,30} These conflicting findings may be explained in part by differences in the severity of hypothyroidism in the study groups or differences in the methods used to assess adrenergic responsiveness. For example, the use of catecholamine infusion may lead to downregulation of the receptors under study, a phenomenon that is unlikely to occur after bolus injections.

**Myocardial Contractility**

In 1967, Buccino et al\textsuperscript{31} examined the effects of thyroid hormones on the intrinsic contractile properties of isolated cat papillary muscles and cardiac energy phosphate stores obtained from myocardial biopsies. They correlated these results with hemodynamic measurements obtained in the intact animal. Compared with muscles from euthyroid animals, muscles from hyperthyroid cats showed a significant increase in both shortening velocity and tension development. The opposite changes occurred in muscles isolated from hypothyroid animals. These changes were not related to contraction frequency, altered cardiac norepinephrine stores, or high-energy phosphate compounds stores. These findings were confirmed in intact dogs\textsuperscript{32} and in humans\textsuperscript{33} using measurements of systolic time intervals, cardiac output, and oxygen consumption. In humans, administration of reserpine to deplete cardiac norepinephrine stores did not alter the effect of thyroid hormones on contractility. Taken together, these findings suggest that thyroid hormones have effects on myocardial contractility that are independent of catecholamines.

In 1982, Forfar et al\textsuperscript{34} studied hypothyroid\textsuperscript{34} and hyperthyroid patients\textsuperscript{35} the effects of exercise and $\beta$-adrenergic blockade on left ventricular function assessed by radionuclide ventriculography. Resting left ventricular ejection fraction was reduced in hypothyroid patients and increased after replacement therapy. Conversely, resting left ventricular ejection fraction was increased in hyperthyroid patients and decreased to normal values in the euthyroid state. In hyperthyroidism, left ventricular ejection fraction responses to both exercise and $\beta$-adrenergic blockade with propranolol were similar before and after thyroid hormone substitution. Furthermore, propranolol did not alter the exercise-induced change in left ventricular ejection fraction in hyperthyroidism. These data appear to favor the concept of a direct rather than a sympathetically mediated effect of hyperthyroidism or hypothyroidism on myocardial function. Yet, it cannot be inferred from these data that thyroid hormones have a direct effect on the heart rather than on the peripheral circulation. Indeed, Wieshammer et al.\textsuperscript{36} studying nine athyreotic patients, have reported decreased cardiac performance that was primarily related to alterations in loading conditions and exercise heart rate. In this model of short-term hyperthyroidism, ejection fraction, systolic pressure/volume relation, and pulmonary capillary wedge pressure were similar at rest and during exercise in both hypothyroid and euthyroid states.\textsuperscript{36}

Echocardiography studies\textsuperscript{37} found a correlation between thyroid hormone levels and velocity of circumferential fiber shortening. In hyperthyroid patients studied before and after treatment, Feldman et al\textsuperscript{38} found a strong correlation between left ventricular contractility and serum thyroid hormone levels. These findings provide additional evidence for a direct inotropic action of thyroid hormones since the observed changes in left ventricular ejection fraction were not associated with alterations of ventricular loading conditions. Left ventricular end-diastolic dimension and end-systolic wall stress remained unchanged after treatment for hyperthyroidism.\textsuperscript{38} However, contractile reserve may be decreased in hyperthyroid patients. This concept has emerged from the observation that left ventricular ejection fraction, although elevated at rest in these patients, does not increase further during exercise.\textsuperscript{35}

The biochemical mechanisms responsible for the intrinsic effect of thyroid hormones on cardiac contractile properties are mediated by specific nuclear receptor proteins. In concert with other nuclear factors, these receptors control thyroid hormone-responsive genes, in particular, the myosin isoenzymes. In hyperthyroidism, myosin isoenzymes are predominantly present as the slowly contracting $\beta$ forms, whereas $T_3$ induces a shift to the more rapidly contracting $\alpha$ forms.\textsuperscript{39} However, this does not apply to all animal models and has not yet been demonstrated in humans. However, Morkin et al\textsuperscript{40} reported in rats with chronic heart failure after myocardial infarction that alterations in cardiac function following thyroid hormone administration precede changes in myosin isoenzyme shifts, suggesting that other mechanisms are involved.

Thyroid hormones also are among factors able to induce the cardiac-specific slow sarcoplasmic reticulum
calcium–ATPase, which, in turn, affects the velocity of diastolic relaxation. Moreover, Ojamaa et al reported recently that thyroid hormone effects on cardiac gene expression may be independent of protein synthesis and cardiac growth. Using Klein and Hong's double-heart model, they showed that \( T_4 \) is capable of directly altering the expression of \( \alpha \)-myosin heavy chain and sarcoplasmic reticulum \( Ca^{2+} \)-ATPase in the unloaded heterotopic isografted heart. These effects of thyroid hormones and certainly other yet unknown ones may be responsible for the complex inotropic and chronotropic effects of thyroid hormones.

**Left Ventricular Diastolic Properties**

Left ventricular filling may be influenced by left ventricular hypertrophy, diastolic relaxation, and preload, all of which can be altered by thyroid hormones. Left ventricular hypertrophy in hyperthyroidism might be related either to \( T_4 \)-induced stimulation of myocardial protein synthesis or to increased cardiac work load. To evaluate the relative importance of these two factors in causing cardiac hypertrophy, Klein and Hong have used an animal model with two hearts—the in situ heart and an infrarenal isograft. The rationale was that both hearts were subjected to the same degree of thyroid hormone stimulation, but only the in situ heart was exposed to the thyrotoxicosis-induced increase in hemodynamic work load. In this elegant study, \( T_4 \) administration significantly increased total weight and myosin content of the in situ working heart but not of the nonworking transplanted heart. These results lead to the concept that thyroid-induced cardiac hypertrophy is caused mainly by an increase in cardiac work load.

This concept has recently been challenged by Bedotto et al. They found that in rats, thyroid hormone–induced left ventricular hypertrophy and increased left ventricular contractility were not attenuated when the \( T_4 \)-induced increase in cardiac work load was prevented by concomitant propranolol, captopril, or hydralazine administration. Thus, these authors concluded that in hyperthyroidism, cardiac hypertrophy is a distinct entity caused by thyroid hormone–induced stimulation of protein synthesis. This interpretation would be consistent with the finding that thyroid-induced cardiac hypertrophy, at least in several animal species, is characterized by specific qualitative changes in myosin isoforms.

Left ventricular diastolic function has also been assessed in hyperthyroid patients, who show no evidence of thyroid-induced left ventricular hypertrophy. In such patients, Mintz et al used two-dimensional echocardiographic Doppler to study various parameters of diastolic function such as isovolumic relaxation time, duration of early diastolic flow velocity, and deceleration time of early diastolic filling. Patients were studied at the time of diagnosis, after 2 weeks on propranolol, and after 4–6 months while euthyroid. Even though propranolol decreased heart rate to euthyroid values, it did not slow the isovolumic relaxation time that remained markedly accelerated. These findings are consistent with the concept that thyroid hormones enhance left ventricular diastolic function independently of adrenergic mechanisms and heart rate. The enhanced diastolic relaxation rate associated with thyroid stimulation may be secondary to the augmented activity of the sarcoplasmic reticulum calcium ATPase pump. However, it is of note that in hyperthyroid patients with left ventricular hypertrophy, diastolic filling may be impaired because beneficial effects of improved relaxation are offset by increased left ventricular stiffness.

In hyperthyroidism and myxedema, reversible diastolic abnormalities have been reported. In an echocardiographic study, asymmetric septal hypertrophy was found in 17 of 19 patients, and some of them had echocardiographic features similar to those found in hypothyroid obstructive cardiomyopathy. In 10 such patients, this abnormality resolved on return to euthyroid state. There is no good explanation for this finding that has been confirmed on postmortem examinations and may represent one potential cause of left ventricular diastolic dysfunction in hypothyroid patients. In a study of nine athyreotic patients without preexisting cardiovascular disease, right heart catheterization and radionuclide ventriculography have been performed before and after replacement therapy. Peak filling rate was increased but time to peak filling rate and pulmonary capillary wedge pressure remained unchanged after \( T_4 \) administration. These findings suggest a decrease in the rate of active diastolic relaxation in this human model of short-lived hyperthyroidism. Others have confirmed the presence of a prolonged ventricular relaxation time in hypothyroid patients using left ventriculography or Doppler echocardiography. In hyperthyroidism, abnormalities in diastolic relaxation are thought to be due to decreased activity of sarcoplasmic reticulum calcium ATPase, an enzyme that regulates intracellular calcium uptake.

**Effects on Peripheral Circulation**

Besides their direct effects on the myocardium, thyroid hormones may influence cardiac output by altering preload or afterload. We will briefly discuss the impact of thyroid function on venous return and on systemic blood pressure.

The effects of thyroid function on venous compliance and blood volume are still elusive. In a study by Gay et al, compared with controls, hyperthyroid rats displayed an increase in mean circulatory filling pressure, no change in blood volume, and a decrease in venous compliance, whereas hypothyroid rats showed a decrease in mean circulatory filling pressure and blood volume but no change in venous compliance. The same group of investigators, in hyperthyroid calves, also reported increases in mean circulatory filling pressure and decreases in venous compliance, but in this model, they were associated with increased blood volume. Increases in mean circulatory filling pressure in thyrotoxic calves probably were not caused by sympathetic stimulation because sympathetic and ganglionic blockade had no effect on filling pressure.

Studies in humans performed early this century have provided evidence that blood volume is increased in hyperthyroidism and decreased in hypothyroidism. There are no data about the effect of thyroid hormones on venous compliance in humans.

In contrast to venous compliance and blood volume, several studies examined the effects of thyroid hormones on peripheral resistance. Theilen and Wilson studied the effects of phenylephrine infusion on cardiac index in thyrotoxic patients and in controls pretreated
with atropine. They found that during phenylephrine infusion, only hyperthyroid patients showed a decrease in cardiac output, suggesting that the increased cardiac output at baseline was due, at least in part, to peripheral vasodilatation. Such vasodilatation may be related to heat production and relative tissue hypoxia caused by increased tissue metabolism. This interpretation would be consistent with the observation in hypothyroid patients of an increased peripheral resistance and a low cardiac output, the latter being directly related to decreased oxygen consumption.61

Thyroid dysfunction also may alter blood pressure. Hyperthyroidism, generally has only minor effects on mean arterial pressure because increases in systolic blood pressure, caused by increased stroke volume, are offset by decreases in diastolic blood pressure, due to peripheral vasodilatation.62 Conversely hypothyroidism has been reported to be associated with increases in diastolic blood pressure.63,64 For example, in a study of 40 hyperthyroid patients overtreatment that resulted in hypothyroidism was associated with an increase in diastolic blood pressure that was reversible when thyroid function returned to normal.65 In a survey of 688 consecutive hypertensive outpatients, 3.6% were found to be hypothyroid,66 and in this subset, diastolic blood pressure fell significantly after adequate thyroid replacement suggesting a cause-and-effect relation. Hormonal profiling revealed that more than half of these hypothyroid hypertensive patients displayed low plasma renin activity, a finding also reported by others.65,66 Low angiotensin levels have also been reported in hypothyroidism.67 These observations suggest that renin, angiotensin, and aldosterone play a minor role in this form of hypertension.68 In contrast, sympathetic activation that has been consistently reported in hypothyroid patients61,68,69 may play a role in sustaining high diastolic blood pressure. However, the above-mentioned alterations in renin-angiotensin and aldosterone may contribute to the expanded plasma volume of hyperthyroidism and the opposite effects in hypothyroidism.

Prohormone atrial natriuretic peptides and atrial natriuretic factor (ANF) are decreased in hypothyroid patients, whereas patients with hyperthyroidism display a marked increase in the levels of these peptides.70 This increase may be due to a direct effect of T4 on ANF mRNA transcription and ANF synthesis as shown in vitro.71 Nonetheless, ANF does not appear to play a key role in systemic blood pressure control.72 Finally, vasopressin may contribute to the increased peripheral resistance seen in hypothyroidism because plasma levels have been reported to be mildly increased and to return to normal after replacement therapy.73

**Chronotropic Effect**

The well-known positive chronotropic effect of thyroid hormones is not found in all models of hyperthyroidism and does not appear to parallel their positive inotropic effect. Marcus et al.74 using an isolated rat heart model, found no significant increase in heart rate in 1-thyroxine-treated hearts compared with controls but a significant difference in contractility. This study suggests that in vivo factors, such as the interaction with the autonomic nervous system, act synergistically to produce a hyperthyroid-related tachycardia.75 However, other groups have come to a different conclusion, suggesting a direct chronotropic effect of T3. In their double-heart model discussed earlier, Klein and Hong found that T3 increased similarly the heart rate of the denervated infrarenal and the innervated in situ hearts.46 In another study, Valente et al.76 found that heart rate in both thyroidectomized and hypothyroidized rats decreased similarly and proportionally to thyroid hormone levels but independently of thyroid stimulating hormone levels. In the same study, the effects of thyroidectomy and chemical sympathectomy on the heart were compared in two groups of rats. The group with thyroidectomy had a significantly slower heart rate than the group with sympathectomy. However, both groups responded with a similar increase in heart rate after treatment with T3.76 These data suggest that thyroid hormones have a direct chronotropic effect. This interpretation is supported by three lines of evidence. First, in vitro studies using preparations of rabbit sinoatrial node and atrial fibers found that thyroid hormones decrease the duration of the repolarization phase of the membrane action potential and increase the rate of the diastolic depolarization and therefore the rate of contraction.76-78 Second, studies using an isolated, perfused heart model found that hearts from animals with experimental hyperthyroidism show increased heart rates and shorter mean effective refractory periods79 than hearts from euthyroid animals. Finally, in isolated hearts from euthyroid animals, addition of T3 to the perfusate stimulates heart rate and shortens refractory period. The mechanism by which thyroid hormones induce these electrophysiological changes is still elusive but may be related in part to their effects on sodium pump density80 and enhancement of Na+ and K+ permeability.81 In humans, chronotropic effects of thyroid hormones have been assessed using 24-hour ambulatory ECG recordings. Hyperthyroid patients show an increase in heart rate throughout sleeping and wake hours,82 whereas in hypothyroid patients a decrease in basal, average, and maximal heart rates was found even though most of them were not bradycardic at rest.83 After treatment, heart rates in both groups returned to normal.82,83

**Arrhythmias**

Thyroid hormones have been shown to alter cardiac excitability, which may lead to arrhythmias. Atria are more sensitive than ventricles to the action of thyroid hormones.77,78,82 Typical arrhythmias found in hyperthyroidism are atrial premature contractions or atrial fibrillation, the latter occurring in 9-22% of patients.84 Conversely, ventricular premature contractions are rare in this setting, and if present, their frequency is not decreased after treatment.85 Malignant arrhythmias such as ventricular tachycardia or fibrillation are exceptional and usually occur only in patients with marked heart failure or associated cardiac disease. The preferential atrial arrhythmogenic effect of thyroid hormones could be due to many factors including the higher β-adrenergic receptor density found in this chamber85 and differences in autonomic innervation between atria and ventricles. It is also possible that the sensitivity of atrial or ventricular myocardial cells to thyroid hormone differ. Whatever the precise underlying mechanism for this difference, the sparing of the ventricles to the arrhythmogenic effects of thyroid hor-
Thyroid Dysfunction and Heart Failure

The above-mentioned effects of thyroid hormones on left ventricular contractility, diastolic function, peripheral resistance, heart rate, and cardiac excitability may rarely concur to induce cardiac failure in both hyperthyroid and hypothyroid patients.

In hyperthyroidism, heart failure may occur in the absence of underlying heart disease as reported in children by Cavallo et al.92 Heart failure also can be the only clinical manifestation of hyperthyroidism, particularly in the elderly with the so-called apathetic form of hyperthyroidism.86 Reduced left ventricular contractile reserve may impair the ability to raise cardiac output to meet the increase of peripheral metabolic demand. Left ventricular hypertrophy, in particular when associated with accelerated heart rate and decreased left ventricular filling time, may result in impaired left ventricular filling. Atrial fibrillation may further compromise left ventricular filling because of the loss of the atrial contribution and a rapid ventricular response rate. Furthermore, decreased systemic resistance, increased blood volume, and venoconstriction, although not documented in humans, may lead to increased venous return, which may occasionally overwhelm cardiac capacity and cause high output failure. In addition, when increases in myocardial oxygen demand due to increased work load and direct effect of thyroid hormones cannot be matched by coronary vasodilation, myocardial ischemia may ensue, particularly in the presence of coronary artery disease or spasm,93 and may contribute to the occurrence of heart failure.

Hypothyroidism may also rarely be the sole cause of heart failure. Recently, one such case has been reported.94 A low heart rate, decreased myocardial contractility, and increased peripheral resistance can all lead to low cardiac output. Furthermore, left ventricular filling may be impaired by the simultaneous presence of left ventricular hypertrophy, abnormal relaxation, and bradycardia. Heart failure may occur when peripheral metabolic demand cannot be matched by an adequate cardiac output. In addition, cardiac tamponade may be a rare cause of cardiac failure in myxedematous patients.96 Heart failure is, however, more common in patients with underlying cardiac disease. Because hypothyroidism is often associated with hypercholesterolemia, coronary artery disease is common in this population, although this has not been confirmed in an autopsy series reported by Steinberg.97 Heart failure may be the result of patchy myocardial necrosis or ongoing ischemia, which may worsen at the time of thyroid replacement therapy, due to increased myocardial oxygen demand in the face of decreased coronary reserve.

Summary

Cardiovascular manifestations are a frequent finding in hyperthyroid and hypothyroid states. In this review, potential mechanisms by which thyroid hormones may exert their cardiovascular effects and pathophysiological consequences of such effects are briefly discussed. Two major concepts have emerged about how thyroid hormones exert their cardiovascular effects. First, there is increasing evidence that thyroid hormones exert direct effects on the myocardium, which are mediated by stimulation of specific nuclear receptors, which in turn leads to specific mRNAs production. Furthermore, there is some evidence that thyroid hormones may also activate extranuclear sites and may directly alter plasma membrane function. Second, thyroid hormones interact with the sympathetic nervous system by altering responsiveness to sympathetic stimulation presumably by modulating adrenergic receptor function and/or density.

Pathophysiological consequences of such direct and indirect thyroid hormone effects include increased myocardial contractility and relaxation that may be related to stimulation by T3 of specific myocardial enzymes. However, when left ventricular hypertrophy occurs in association with hyperthyroidism, it may be related to either direct thyroid hormone–induced stimulation of myocardial protein synthesis or to thyrotoxicosis-induced increases in cardiac work load. Although hyperthyroidism generally has little or no effect on mean arterial blood pressure, hypothyroidism is often associated with increases in diastolic blood pressure that are reversible after hormone substitution and may be mediated in part by sympathetic activation. Moreover, there is increasing evidence that thyroid hormones have direct chronotropic effect on the heart that are independent of the sympathetic nervous system. Finally, thyroid hormones may trigger arrhythmias mostly at the level of the atria, and there is some evidence that tissue hypothyroidism may increase the fibrillation threshold of the ventricles. However, there are no clear data in humans indicating that hypothyroidism confers a protection against ventricular or atrial arrhythmias.

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