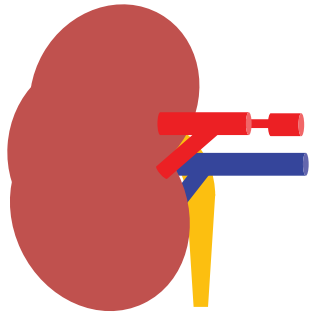

FIGURE 7.8 In the 2K1C model of hypertension, surgical constriction of the renal artery leads to chronically increased blood pressure (hypertension) that plateaus 2–3 weeks after surgery.

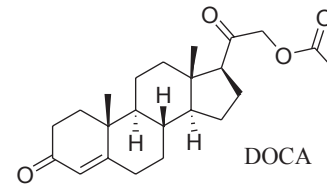

FIGURE 7.9 Prolonged exposure to mineralocorticoids such as deoxycorticosterone acetate (DOCA) produces hypertension in several useful animal models.

particularly deoxycorticosterone acetate (DOCA, Figure 7.9). Prolonged exposure to mineralocorticoids (2–4 weeks) causes hypertension in rats, dogs, and pigs that are characterized by increased cardiac output and volume expansion. In some cases, animal model performance can be improved by feeding them a high-salt diet. Similar results can be obtained in mice if the mineralocorticoids are replaced with glucocorticoids.[25] Simple dietary intervention can also be used to induce hypertension under the correct circumstances. The Dahl salt-sensitive rat, for example, will develop hypertension in as little as 3 weeks if fed a high-salt diet.[26]

Genetic manipulation, either via selective breeding or transgenic science, has also provided a number of animal models of hypertension. The most recognized of these is the spontaneously hypertensive rat (SHR). This model of hypertension was developed by selective breeding of Wistar rats that naturally demonstrated high blood pressure. Hypertension begins to develop 5–6 weeks of age, and cardiovascular disease becomes apparent at 40–50 weeks. The SHR has been extensively used in the study of hypertension.[4,27]

Irrespective of how an animal model of hypertension is generated, a method of reliably measuring blood pressure that will not in itself cause blood pressure to spike (e.g., fear or anxiety related increases) must be established. In the absence of such a method, a compound's ability to lower blood pressure might be masked by an increase in blood pressure related to the measurement itself. Training of animals to tolerate the application of a blood pressure cuff, which often requires restraining the animal, requires an initial training period of 1–2 weeks. In rats and mice, a tail blood pressure cuff is employed, while larger animals can be assessed on limbs. Once the animals are trained, blood pressure readings can be obtained in the presence and absence of a test compound to assess efficacy.[28]