control induced by radiation, whereas chemotherapy is intended for metastases. Associated chemotherapy may also have a direct effect on the tumor cells by enhancing their radiosensitivity.

Radiotherapy can be defined as the medical use of ionizing radiation for the purpose of cancer treatment. It is based on the generation of hydroxyl radicals from homolytic fragmentation of water molecules upon local application of ionizing radiation. This fragmentation can be preceded by ionization of water molecules (Figure 4.42a) or by their excitation (Figure 4.42b).

As previously mentioned, the main mechanism of cytotoxicity of hydroxyl radicals is based on the generation of radicals from biomolecules (Figure 4.43a). Cellular defenses against this process are varied, but they are normally based on the reaction of these radicals with an antioxidant molecule such as glutathione, which reacts with the biomolecule radicals, repairing them and leading to a glutathione radical. The latter species is harmless despite being a radical because of its tendency to dimerize to a disulfide (Figure 4.43b).

Damage by ionizing radiation is enhanced by the presence of oxygen by a factor of 2- to 3.5-fold; therefore, oxygen can be considered to act as a very efficient radiosensitizer. In fact, hypoxic cells in tumors are resistant to radiotherapy, with increased resistance to ionizing radiation being observed at oxygen concentrations of less than 1% (8 torr).[114] For the same reason, patients with low hemoglobin levels often do not show a good response to radiotherapy. This so-called "oxygen effect" is due to the property of oxygen of reacting with biomolecule radicals to generate other radicals that cannot be repaired because their reaction with glutathione does not lead back to the biomolecule but, rather, to an oxidized derivative (Figure 4.44).

Radiotherapy can be applied using several methods, which are summarized here.

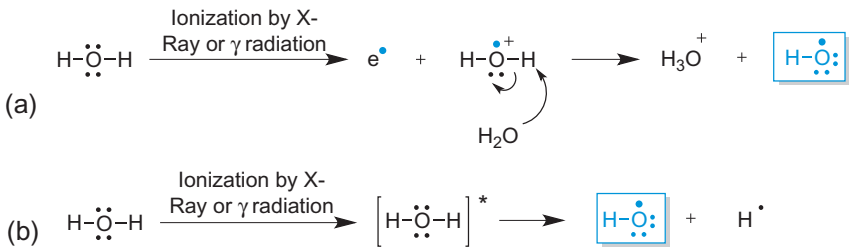

FIGURE 4.42

Generation of hydroxyl radicals from water during radiotherapy.

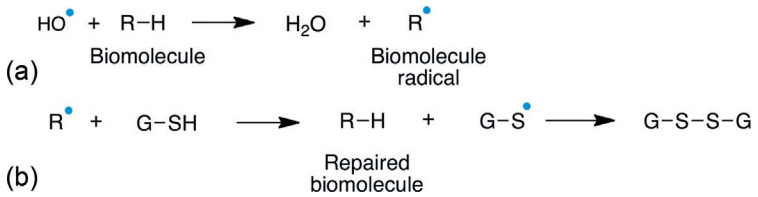

FIGURE 4.43

Repair of biomolecule radicals by glutathione.