but past this point the absorption curve for a gas or vapor of low reactivity becomes rather flat. With a relatively water-insoluble vapor such as benzene, blood saturation occurs so rapidly that even the venous blood may reach 70 to 80 per cent of saturation within 30 minutes, yet relatively complete saturation may require as much as 2 or 3 days. This can be explained by the fact that the fatty tissue, which has the greater affinity for benzene, removes and stores the benzene carried by the blood, but this fatty tissue has in many instances a very meager blood supply and therefore requires a longer period to attain equilibrium.

Methanol is typical of vapors highly soluble in water. About 24 hours inhalation of this vapor is required before the blood is 70 per cent saturated (about 50 times as long as for a similar percentage saturation with benzene), yet relatively complete saturation here requires little longer than with benzene, the difference being that the fatty tissues with their smaller blood supply are not a reservoir for methanol, and distribution throughout the body at equilibrium is directly proportional to the water content of each tissue. Both benzene and methanol are examples of very slightly reactive vapors.

Carbon disulfide, approximately 90 per cent of which has been found to be metabolized, may be cited as an example of a moderately reactive, relatively water-insoluble vapor. McKee and associates[9] have reported upon the blood saturation with carbon disulfide in inhalation exposures of dogs. From its physical and chemical properties, carbon disulfide would be expected to have an absorption curve resembling that for benzene except for the effect of a higher rate of metabolism, and McKee's data indicate that this is the case. If the points on his graph for the blood saturation of a dog breathing 50 p.p.m. carbon disulfide are connected by an exponential curve, the data indicate a saturation of around 90 per cent at the end of a 3½-hour exposure. The coefficient of distribution of CS_2 between blood and room air at this percentage saturation was 4.3 on a milligrams per liter basis.[10] If this were corrected for alveolar air temperature and humidity, the value at equilibrium would be approximately 5. Desaturation was rapid and, for single exposures, more or less complete within 2 to 6 hours. This is similar to the desaturation curve for benzene. During accumulation or absorption the arterial blood is saturated to a higher degree than venous blood, while at equilibrium or saturation the concentration is the same in each, and during elimination the concentration of benzene in the arterial blood is lower.

The difference in vapor concentration between arterial and venous blood is dependent upon the solubility or coefficient of distribution of the particular vapor. With a very soluble vapor the difference is negligible, while with a slightly soluble vapor, such as benzene, the difference is marked, and during accumulation the arterial blood, once the lungs are filled with vapor by the first few inhalations, is equilibrated with air only slightly less in concentration of vapor than the air inhaled.

[9] R. W. McKee, C. Kiper, J. H. Fountain, A. M. Riskin, and P. Drinker, *J. Am. Med. Assoc.*, **122**, 217 (1943).

[10] R. W. McKee, private communication.

In other words, the blood passing through the lungs is not sufficient to absorb an appreciable percentage of the vapor from the alveolar air. This has an important bearing on brief exposures to high concentrations of slightly soluble vapors. The arterial blood supply to the brain is large: therefore, brief exposures to high concentrations of anesthetic gases or vapors of low solubility produce rapid effects even though the degree of saturation of the body is very low. The administration of ether is a good example of this point. Moderate concentrations may be given that will induce unconsciousness after ½ hour or more and the effects will be somewhat prolonged, or concentrations may be given sufficiently high to induce unconsciousness quickly and have recovery occur shortly after removal from exposure, providing the exposure has not been prolonged. This also has a practical bearing in degreasing work where a short exposure to high concentrations of trichloroethylene, or another similar solvent, may not materially raise general body concentration but may induce anesthesia. It is therefore important to know peak as well as average vapor concentrations.

The curves in Figure 2 illustrate the differences in rate of absorption by inhalation and in approach to equilibrium in the circulating blood for different classes of gases and vapors. Nitrogen, nonreactive and slightly soluble, but with some specific affinity, approaches equilibrium rapidly (see also page 588). Carbon disulfide, moderately reactive and slightly soluble, approaches saturation rapidly, but data are lacking on the period of complete saturation. Benzene, very slightly reactive and slightly soluble, reaches 70 per cent saturation rapidly but does not attain complete equilibrium even after a period of 3 days. Methanol, a slightly reactive, highly soluble vapor, gradually approaches saturation, requiring about 24 hours for 70 per cent saturation and about 5 days for essentially complete saturation. Ethanol (not shown) attains saturation slightly more slowly than does methanol because it is metabolized fairly rapidly.

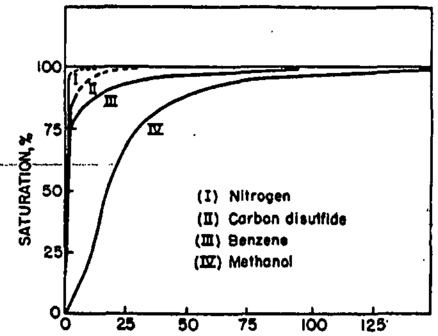

Figure 2. Curves illustrating the absorption of some representative gases and vapors into the blood of living dogs.