Editorial

Uptake of solvents from the lungs

On the basis of their solubility in blood and tissues, the solvents may be ranked with the most soluble substances at one extreme and the least soluble at the other. Among the readily soluble substances are compounds such as xylene, styrene, acetone, and butyl alcohol (group 1) whereas among the less soluble substances are methyl chloroform, methylene chloride, trichloroethylene, and toluene (group 2).¹ The solubility of a solvent has great importance for the uptake from the lungs and for the accumulation in the body during exposure. Other factors, however, are also important, including pulmonary ventilation and blood circulation which influence the transportation rate to and from the lungs and other tissues. The degree of physical activity must also be considered in connection with these factors and the biotransformation of the solvent is another important factor.

I will discuss the difference in the uptake of substances in the two groups during resting conditions and during exercise at different work rates, implying systematic changes in pulmonary ventilation and blood circulation. At rest, the relative uptakes—that is, the percentage uptakes—are somewhat higher for solvents in group 1 than in group 2, although the differences are comparatively small.²

During exercise, with increased pulmonary ventilation and blood circulation, the differences are much more pronounced. The uptake of styrene is typical for solvents in group 1.³ Exercise results in increased pulmonary ventilation and thereby an increased supply of styrene to the lungs. The uptake correlates well with the pulmonary ventilation or alveolar ventilation and is enhanced five to six times during the heaviest work load (150 watts), although the percentage uptake remains fairly constant. The uptake of methylene chloride is typical for solvents in group 2. The uptake is, on average, doubled by a work load of 50 watts but further increase in work load has little or no effect on pulmonary uptake.⁴ Whereas pulmonary uptake remains fairly unchanged, at 150 watts the percentage uptake decreases from 55% at rest to 23%. In a fairly thin subject exposed to trichloroethylene the percentage uptake declines throughout an exposure period of 140 minutes, from approximately 55% at rest to 6% at 150 watts and is almost zero at the end of exposure.⁵

To understand these findings it is necessary to introduce the concept of the partition coefficient.¹ The blood air partition coefficient of a solvent describes the distribution of the solvent between blood and air when equilibrium has been reached. Similarly, the tissue blood partition coefficient describes the ratio between the tissue and blood concentrations at equilibrium. The higher the blood air partition coefficient the more of the solvent is dissolved in blood in relation to the concentration in air. For example, a blood air partition coefficient of 10 means that when a concentration of the solvent of 5 vol% is present in the alveoli the concentration of the solvent in blood would be 50 vol% at equilibrium.

The difference in uptake between the two groups of solvents is caused by different equilibration rates in the tissues. Owing to the high solubility of the solvents (high partition coefficients) in group 1, the tissues have a great capacity to retain them and no tissue approached equilibrium with the blood during the experimental exposures referred above. Thus the tissue uptake of group 1 solvents is mainly flow limited so that when pulmonary ventilation and blood circulation are increased, tissue blood flow and hence tissue uptake are enhanced.

The capacity of the tissues to retain solvents included in group 2 is less. After 30 minutes of resting exposure, well perfused tissues are almost equilibrated but the concentration in muscles and fat is low owing to perfusion limitation. Therefore, the increase of pulmonary uptake during exercise is attributed mainly to increased uptake only in those tissues in which perfusion is enhanced by exercise. It may be assumed that after 30 minutes of exercise at 50 watts the exercising muscles probably approach equilibrium. Therefore, a further increase in the work rate would enhance uptake mainly in the adipose tissues. Since only a relatively small fraction of cardiac output is distributed to adipose tissues, the pulmonary uptake increases very little.

The biotransformation of a solvent, the major part of which takes place in the liver, is also important for its uptake.⁶ At rest, approximately 25% of the cardiac output is distributed to the liver, and this amount of blood may be cleared of a solvent. If the extraction is complete the concentration in mixed venous blood will decrease by 25% as the result of biotransformation and accordingly, the uptake tends to increase by 25%. This means that the blood flow to the liver and the rate of biotransformation are important for the decrease in the solvent concentration in mixed venous blood. When the other organs are equilibrated, uptake from the lungs will continue with a rate equal to the rate of biotransformation in the liver. Extrahepatic elimination of a solvent is

also important in this context.

Heavy exercise decreases hepatic blood flow.² The reduced pulmonary uptake of highly metabolised solvents, such as styrene, trichloroethylene, and methylene chloride, noted during heavy exercise may therefore be partially caused by the reduced rate of biotransformation resultant upon the reduction in hepatic blood flow.

The examples quoted above all concern solvents that are highly lipid soluble but less soluble in water. With exposure to water soluble substances the results are somewhat different. With acetone, which is highly hydrophilic, the relative uptake is 45% irrespective of time and work load—that is, physical exercise does not change the percentage uptake from the lungs.⁷ The total uptake thus increased linearly with enhanced pulmonary ventilation and blood circulation during step wise increases in work load. The concentration in the blood increases linearly with the increased uptake from the lungs, but the percentage uptake values are low considering the high blood solubility. Much higher uptake values have been found for less soluble substances.

The explanation of this phenomenon may be as follows. When a water soluble substance passes the respiratory dead space the vapour will be dissolved partly in the saliva and partly in the water of the respiratory epithelium. Therefore, the concentration of acetone in the inspired air will decrease during the passage down to the alveoli. When the alveolar air passes the epithelium during expiration, acetone will be partially desorbed. Consequently, less acetone will reach the alveoli and the net uptake will be comparatively low. As a result, the concentration of acetone in expired air will be higher than in the alveolar air.

Uptake from the alveoli will continue until the concentration of the solvent in mixed venous blood is equal to that in arterial blood. As mentioned above the biotransformation of the solvent will continuously decrease the concentration in the hepatic and the mixed venous blood allowing a continuous uptake from the lungs. Furthermore, the fat tissues will be equilibrated very slowly owing to their low perfusion rate and the high lipid solubility of the solvents.⁸ Therefore, the blood returning from fatty

tissue will decrease the concentration in venous blood and influence the uptake from the lung for an extended period. The rate of uptake by the fat varies considerably, however. The concentration of toluene in subcutaneous fat has been studied in two series of experiments, each with an exposure period of two hours.⁹ Resting exposure gave a peak concentration of approximately 2 mg/kg; the concentration after 50 watt exercise was 10 times higher. The explanation is probably that the perfusion of the subcutaneous fat was increased during 50 watt exercise because of increased fat metabolism.

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