제 목	국 문	PB-PK 모델을 이용한 톨루엔의 생물학적 폭로지표 개발
	영 문	Simulation of Toluene in Venous Blood with a Physiologically Based Pharmacokinetic Model : Its Application to Biological Exposure Index Development
저자 및 소속	국 문	장 재연, Pierre O. Droz* 아주대학교 의과대학 산업의학교실 *스위스 로잔 의과대학 산업보건연구소
	영 문	Jae-Yeon Jang, Pierre O. Droz* *Dept. Occupational and Environmental Medicine, Ajou Univ.* **Institute of Occupational Health Science, Univ. of Lausanne*
분 야	산업 보건	발 표 자 : 장 재 연
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1. Objective

The recent reduction of the threshold limit value(TLV) of the American Conference of Governmental Industrial Hygienists(ACGIH) for toluene to 50 ppm called for a redefinition of the corresponding Biological Exposure Indices(BEIs).

This study was done in order to present an example of the contribution of physiologically based pharmacokinetic(PB-PK) model to the development of Biological Exposure Indices.

2. Method

The PB-PK used in this study consist of 7 compartments representing the different tissues. Toluene absorption and elimination is calculated based on tissue volumes, blood perfusions, partition coefficients and alveolar ventilation. For metabolism, the model has been transformed to include non-linear. Michaelis-Menten kinetics. The model differential equations are solved by a program written in Basic.

All simulations were done for a standard man(170cm, 70kg) exposed in standard working condition (8 hours/day with 1 hour break, 5 days/week). The workload was assumed to be 50 W during the workshift and 0 W during the non-exposure time, respectively.

3. Result

The comparison of the simulation results for several biological indicators with measurements in workers showed a good agreement.

Excluding Tuesday morning, venous blood concentration of toluene in a morning range from 0.07 to 0.09 mg/l for an exposure at 50 ppm with 50 W physical workload. This range can therefore be used as a basis for a BEI for toluene in blood.

The effects of confounding factors, such as exposure fluctuation, physical workload after exposure, and air contamination at the sampling site were also simulated. According to fluctuations of the exposure level within the exposure day, there was big difference in the venous blood toluene concentration at the end of shift but no difference in the venous blood toluene concentration at the next morning. The exercise of 100 W for 1 hour and for 2 hours after work did not have a large effect on the venous blood toluene concentration at the next morning. The concentration of 0.07-0.09 mg/l as proposed for BEI can be reached within 3 minutes of exposure to 50 ppm. The quality control management is therefore critical at sampling.

4. Discussion

The use of a PB-PK model is very helpful in the establishment of BEI. In the present date, no data were available in worker for toluene in venous blood sampled in the morning. A PB-PK model carefully tested makes it possible do predict such missing. An other application of the PB-PK model is the understanding of the influence of confounding factors, such as physical workload after exposure, exposure fluctuation, and air contamination at the sampling site.

The simulation results show that toluene in venous blood sampled in the morning can be reliably used as a determinant to monitor toluene exposure with a Biological Exposure Index based on a 0.07-0.09 mg/l range.