SUPPLEMENTAL MATERIAL

Perinatal Exposure To Low Doses Of Dioxin Can Permanently Impair Human Semen Quality

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CALCULATION OF TCDD ELIMINATION HALF-LIVE FOR MOTHERS USED TO ESTIMATE TCDD CONCENTRATIONS AT THE TIME OF CONCEPTION

The TCDD elimination half-lives used to estimate the TCDD concentrations of the mothers at conception based on their TCDD serum concentrations measured in 1976/1977 after the Seveso accident were calculated using the methods presented in Kreuzer et al. (1997). The total biological half-life for the mothers can be calculated from the metabolic elimination half-life ($t_{m,1/2}$) and the excretion half-life ($t_{f,1/2}$) using the following equation:

$$t_{\frac{1}{2}} = \frac{1}{\left(\frac{1}{t_{m\frac{1}{2}}}\right) + \left(\frac{1}{t_{f\frac{1}{2}}}\right)}$$

Subsequently, $t_{m,1/2}$ can be estimated using the following equation from Kreuzer et al. (1997):

$$t_{m\frac{1}{2}} = t_{m\frac{40,1}{2}} * \left(\frac{V}{V_{40}}\right) * \left(\left[\frac{V_{L,40}}{V_L}\right]\right)^{2/3}$$

Where $t_{m,40,1/2}$ is the metabolic half-life for a 40 year old reference male (10.5 yrs); V is the volume of distribution for the mother (L); V_{40} is the volume of distribution for the 40 year old reference male (21.2 L); V_L is the liver volume of the mother (L); and $V_{L,40}$ is the liver volume of the 40 year old reference male (1.84 L) (Kreuzer et al., 1997).

The excretion half-life ($t_{f,1/2}$) can be estimated using the following equation:

$$t_{f\frac{1}{2}} = \frac{\ln(2) * V}{\frac{dFa}{dt} * \rho_{body}}$$

Where dFa/dt is the mass of lipids excreted per unit time (kg/yrs) and ρ_{body} is the density of the entire body of 1 kg/L).

The volume of distribution for the mother can be estimated from the following equation from Kreuzer et al. (1997):

$$V = V_F + P_{M_{I_F}} V_M + P_{VRG_{I_F}} V_{VRG}$$

Where V_F is the adipose tissue volume (L); V_M is the muscle tissue volume (L); V_{VRG} is the residual tissue volume (L); $P_{M/F}$ is the muscle/fat partition coefficient (0.11 based on Kreuzer et al., 1997); and $P_{VRG/F}$ is the residual tissue/fat partition coefficient (0.05 based on Kreuzer et al., 1997). The adipose tissue volume is estimated from the age and gender-specific adipose tissue weights (kg) from ICRP (1975) by dividing the weight of adipose tissue by 0.92, the density of adipose tissue (Kreuzer et al., 1997). The muscle volume is estimated from the age and gender-specific muscle tissue weights (kg) from ICRP (1975) assuming a muscle density of 1 kg/L. The

residual tissue volume is the volume of tissue that is not adipose or muscle and was estimated using the following equation from Kreuzer et al. (1997):

$$V_{VRG} = 0.9V_{body} - V_F - V_M$$

Where V_{body} is the volume of the whole body (L) and is equal to the body weight divided by the assumed density of a body of (1 kg/L).

Example calculation for 25 year old mother

For a 25 year old mother with a body weight of 60 kg, adipose tissue volume of 15.6 L, and muscle tissue volume of 17.0 L, her residual tissue volume is:

$$V_{VRG} = 0.9(60\ L) - (15.6\ L) - (17.0\ L)$$

$$= 21.4\ L$$

Based on this residual tissue volume, the maternal volume of distribution, V, is:

$$V = (15.6\ L) + (0.11 * 17.0\ L) + (0.05 * 21.4\ L)$$

$$= 18.5\ L$$

The excretion half life, $t_{f,1/2}$, can be calculated as:

$$t_{f\frac{1}{2}} = \frac{\ln(2) * (18.5\ L)}{\frac{\left(1.546\frac{kg}{yr}\right)}{1\frac{kg}{L}}}$$

$$t_{f\frac{1}{2}} = 8.29\ yrs$$

And the metabolic half-life, $t_{m,1/2}$, can be calculated as:

$$t_{m\frac{1}{2}} = (10.5\ yrs) * \left(\frac{18.5}{21.2}\right) * \left(\left[\frac{1.84}{1.44}\right]\right)^{2/3}$$

$$t_{m\frac{1}{2}} = 15.0\ yrs$$

The overall elimination half-life can then be calculated as:

$$t_{\frac{1}{2}} = \frac{1}{\left(\frac{1}{15.0\ yrs}\right) + \left(\frac{1}{8.29\ yrs}\right)}$$

$t_{\frac{1}{2}} = 5.33\,yrs$

References

ICRP (International Commission on Radiological Protection). 1975. No. 23 Report of the Task Group on Reference Man. New York:Pergamon Press.

Kreuzer PE, Csanády GA, Baur C, Kessler W, Päpke O, Greim H, et al. 1997. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and congeners in infants: A toxicokinetic model of human lifetime body burden by TCDD with special emphasis on its uptake by nutrition. Arch Toxicol 71:383-400.