Russian phenoxy herbicide production workers: exposure to and elimination of dioxins

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Abstract

Additional exposure and some elimination data have been obtained on a cohort of chemical workers who produced phenoxy herbicides and other chemicals in the 1960's in Ufa, Russia. From samples taken in September 1992 and analysed recently, blood lipid concentrations of 2,3,7,8-TCDD for 14 workers who produced 2,4,5-T averaged about 300 ng/ kg, more than double that previously reported from this same cohort. Those workers who produced 2,4-D had high 1,2,3,7,8-PnCDD and even the blood of administrative personnel contained notably greater blood levels of 2,3,7,8-TCDD and TEQ than normal. Elimination of this body burden for 4 of six 2,4,5-T workers was similar to that reported elsewhere but, for two individuals with relatively low exposure , blood levels appeared to increase somewhat.

Introduction

Chemical workers have long been pivotal in the risk assessment of industrial chemicals since they can be exposed occupationally to higher concentrations of noxious substances than is the general population. Such elevated exposure allows adverse health effects to be detected more readily than otherwise. Previously we published[1-3] on the exposure of a cohort of Russian workers who produced phenoxy herbicides and other chlorinated substances in the 1960's in the city of Ufa, Bashkortostan Republic. In a period of two years or so in 1965-7, about 250 workers produced 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). Some 78 males worked for the entire two year period at this one task and overall 128 workers were diagnosed with chloracne. All of the 2,4,5-T individuals whose blood was tested had elevated levels of dioxins particularly 2,3,7,8-TCDD more than two decades after initial exposure. This occupational group was also unique in that both exposure and health effects involved males and females and even children.

Phenoxy herbicide producers and chemical accident victims continue to generate scientific enquiry as evidenced by recent investigations on carcinogenic effects[4] and altered sex ratios[5]. In addition scientific exchange between Russia and American agencies has been fostered in response to changing political situations. For these reasons, we report here a more expanded account of the

chemical exposure of the Ufa Khimprom cohort including some workers who produced chlorinated material other than 2,4,5-T. Data is also given on the elimination characteristics of the workers over a period of about 4 years.

Experimental

Sampling For the exposure characterization reported here, whole blood samples were obtained in September 1992 by one of us (AS) and kept frozen (-18° to -20°C) until analysed in October 1996 to March 1997. The original blood drawing comprised 60 samples divided as follows: i) 34 workers (24♂; 10♀) who produced 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), ii) 8 children (4♂; 4♀) one of whose parents worked with 2,4,5-T, iii) 6 workers (4♂; 2♀) who produced 2,4-dichlorophenoxyacetic acid (2,4-D), iv) 3 female workers who produced the copper salt of 2,4,5-trichlorophenol and 2 female workers from the manufacture of MCPA (2-methyl-4-chlorophenoxyacetic acid), v) non-workers as follows: a) 5 female administrative employees from the factory and b) two pooled control samples from the city of Ufa. Of this total of 60 blood samples, we originally reported[2] results on 21 people; 10 adults (4♂; 4♀) from 2,4,5-T, the eight children of these 10 workers and 3 control (two administrative and one pool) samples. Of the remaining 39 blood samples, this report gives data on 25 new analyses by the Health Canada laboratory including 14 from the 2,4,5-T production, four from the 2,4-D area, three from other chemicals, and four control samples. More recently in 1996, a number of new blood samples were drawn from the same 2,4,5-T workers as reported previously[2] and analytical data carried out by the Bashkirian Ecological Centre are now available on five of these individuals.
Analysis The 25 blood samples taken in 1992 were analysed in 1996-67 by denaturing with ammonium sulfate, solvent extraction with ethanol-hexane, lipid determination gravimetrically, defatting with strong sulfuric acid, purification on adsorbents of acid/base silica and Florisil, and separation of chemical classes on activated carbon. Determination was by gas chromatography-mass spectrometry and quantification by the isotope dilution internal standard method[6]. The five blood samples taken in 1996 for the elimination study were analysed by the Baskortostan Regional Ecological Centre (BREC), Ufa using EPA method 1613[7].

Results and Discussion

A summary of the exposure characteristics of a further 25 workers are given in Table 1 divided among chemical production. The 2,3,7,8-TCDD content of the fourteen 2,4,5-T workers is 2 to 3 times higher than reported previously[2] for 10 workers from this same group (mean about 112 ng/kg). Some of this difference is due to the low lipid content of these 1996-7 analyses which tends to elevate the blood concentration on a lipid basis.. While we are confident that all blood lipids have been extracted from these samples[8], their storage for more than 4 years has resulted in partial degradation of the blood triglyerides[9] even at -18 to -20 °C. Despite this complication, the exposure of the 2,4,5-T cohort is still higher than first reported with women appearing to be greater than men. The blood lipid concentrations of the 2,4-D subgroup is unique in that the most toxicologically significant exposure is for 1,2,3,7,8-PnCDD not 2,3,7,8-TCDD. The data on the two trichlorophenol individuals, while limited, shows the highest TCDD exposure of all. Furthermore, those individuals who worked in administration and not in the factory per se have elevated TCDD and TEQ when compared to contemporary Russian individuals. This result along

with comparison of the job functions of the 2,4,5-T group underlines the fact that job classification and history are often poor surrogates for exposure as defined by blood lipid concentrations. The profiles of the blood samples are generally typical with only 2,3,7,8-substituted PCDDs/PCDFs present. However, two of the blood samples, one from the 2,4,5-T group and the other from the production of 2,4,-D are distinctive. Readily measurably amounts (more than 5 to 10 ppt) of all seventeen 2,3,7,8-substituted PCDDs/PCDFs (seven PCDDs and ten PCDFs) could be detected in these two samples which, to our knowledge, is the first time this pattern with all 17 congeners present has been reported..

Table 2 shows the pharmacokinetic profile for six of the 2,4,5-T workers with blood sampling taken about 4 years apart. For 4 of the 6 individuals (numbers 1 to 4), the t½ for 2,3,7,8-TCDD is in the range of that reported by other investigators. The estimated value for C_0 (concentration at time of first exposure in 1966) of 500 to 1000 ng/kg blood lipid when chloracne was present may be somewhat lower than previously estimated for cohorts in other countries. For two of the 6 individuals (numbers 5 and 6) whose exposure was not particularly elevated in 1992 at the time of first blood drawing, there appears to be a slight elevation in the 2,3,7,8-TCDD content. The reason for this anomaly for those people who now no longer work at this occupation is not certain and may be related to exposure from unspecified sources and to the analytical methods which have been performed by two different laboratories at two separate times.

Table 1: Exposure of Russian chemical workers from Ufa to PCDDs/PCDFs in whole blood samples collected in September 1992 and analysed in 1996-7

	2,3,7,8-TCDD	1,2,3,7,8-PnCDD	TEQ ΣPCDD/PCDF
Production type	ng/kg blood lipid		
2,4,5-T (n=14)	299	93	384
2,4,5-T males (n=10)	214	74	282
2,4,5-T females (n=4)	369	51	417
2,4-D (n=4) 2♂; 2♀	69	195	277
2,4,5-trichlorophenol (n=2) 2♀	578	535	900
MCPA (n=1) ♀	121	146	232
Administrative controls (n=4) 4♀	36	28	66

Table 2: Pharmacokinetics of 2,3,7,8-TCDD and 1,2,3,7,8-PnCDD in six 2,4,5-T phenoxy herbicide workers over a period of 4 years from September 1992

			2,3,7,8-TCDD ng/kg		1,2,3,7,8-PnCDD ng/kg		TEQ (D/F) ng/kg		2,3,7,8-TCDD Kinetics	
No	Sex	Date taken 1996	1992 blood value	1996 blood value	1992 blood value	1996 blood value	1992 blood value	1996 blood value	Half life Years	C_0 1966 ng/kg
1	F	Oct	144	110	17	13	163	133	9.7	889
2	F	Oct	194	170	54	45	230	208	17	535
3	F	May	83	66	19	ND(10)	99	85	9.7	684
4	M	March	78	55	63	41	129	87	6.9	1040
5	F	Nov	61	93	11	28	72	128	neg	--
6	M	-	35	54	34	--	73	214	neg	--

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