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Factors Affecting the Exposure of Ground-rig Applicators to 2,4-D Dimethylamine Salt

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Abstract. This is a report on exposure to and absorption of the herbicide 2,4-D dimethylamine salt by farmers carrying out spray operations with tractor-drawn ground-rigs, involving handling, transferring, mixing, and applying the herbicide to wheat. The 30 individual spray operations lasted 55 to 870 min, and involved 1 to 11 tank fills, and application of 6.7 to 88.3 kg 2,4-D (acid equivalent, a.e.) to 16 to 194 ha.

Air sampling, hand washes and clothing patch techniques served as a basis to calculate the amount of 2,4-D available for inhalation, and deposition on the hands and under the clothing.

The "cumulative potential exposure" was calculated as the total amount of 2,4-D (a.e.) which could have come into contact with the body by both the inhalation and dermal routes of exposure. The calculated amount inhaled accounted for less than 2% of the calculated potential cumulative exposure, while deposition on the hands accounted for 80 to 90% of the potential cumulative exposure. The 2,4-D deposition on the rest of the body ranged from 10 to 20% of the potential cumulative exposure.

Urinary 2,4-D excretion accounted for 1 to 2% of the potential cumulative exposure. The total calculated amount of 2,4-D deposited on the body (minus the hands) and the total amount excreted in the urine were highly correlated with the number of tank fills, area sprayed, amount sprayed, and duration of the spray operation.

Current concerns about the safety of herbicides have led to studies on the exposure hazards to applicators, one of the critical groups directly exposed to herbicides. Exposure estimates have been reported for several classes of herbicides, such as bipyridyls (Chester and Woollen 1982; Wojeck *et al.* 1983), phenoxy acids (Kolmodin-Hedman and Erne 1980; Lavy *et al.* 1980a, 1980b; Draper and Street 1982; Franklin *et al.* 1982; Nash *et al.* 1982; Åkerblom *et al.* 1983; Kolmodin-Hedman *et al.* 1983a, 1983b; Nigg and Stamper 1983), carbamates (Dubelman *et al.* 1982), dinitroanilines (Day *et al.* 1982), and others (Knarr *et al.* 1982; Putnam *et al.* 1983). These studies evaluated diverse types of application equipment, such as fixed-wing aircraft (Lavy *et al.* 1980b; Franklin *et al.* 1982; Nash *et al.* 1982), helicopters (Lavy *et al.* 1980a), tractor-drawn ground-rigs (Kolmodin-Hedman and Erne 1980; Lavy *et al.* 1980b; Draper and Street 1982; Nash *et al.* 1982; Åkerblom *et al.* 1983; Kolmodin-Hedman *et al.* 1983a, 1983b; Putnam *et al.* 1983); mist blowers (Lavy *et al.* 1980a, 1980b), and hand-operated guns, knapsack-type sprayers and similar equipment (Lavy *et al.* 1980a, 1980b; Chester and Woollen 1982; Nigg and Stamper 1983; Wojeck *et al.* 1983).

Available exposure studies vary in their emphasis on the inhalation or dermal exposure routes and in the extent to which they involve determination of herbicide residues in plasma and/or urine samples. Studies of exposure via the inhalation and dermal routes, combined with estimates of absorption based on plasma and/or urine analyses have been made by Lavy *et al.* (1980a, 1980b), Chester and Woollen (1981), Draper and Street (1982), Franklin *et al.* (1982), Nigg and Stamper (1983), and Wojeck *et al.* (1983). Other exposure studies have measured only herbicide concentrations in air coupled with plasma and/or urine analysis as a measure of absorption (Kolmodin-Hedman and Erne 1980;

Kolmodin-Hedman *et al.* 1983a, 1983b; Libich *et al.* 1984). Some studies have measured potential exposure via the inhalation and dermal routes (Dubelman *et al.* 1982; Knarr *et al.* 1982; Putnam *et al.* 1983), or only via the inhalation route (Day *et al.* 1982).

Several factors have been identified as affecting exposure of those handling or using pesticides. Lavy *et al.* (1980a, 1980b); Nash *et al.* (1982); Putnam *et al.* (1983); and Wojeck *et al.* (1983) measured exposure associated with the use of different types of application equipment. The effects of specific tasks, such as those carried out by the mixer, loader, pilot, etc. were evaluated by Lavy *et al.* (1980a, 1980b); Chester and Woollen (1982); Draper and Street (1982); Franklin *et al.* (1982); Knarr *et al.* (1982); Nash *et al.* (1982); and Wojeck *et al.* (1983). Most of these studies suggested that the dermal route was the major pathway for herbicide entry into the human body, with some implying that hands were probably the most heavily exposed parts of the body. The latter was confirmed by studies in which residues on applicators' hands were sampled after each exposure (Draper and Street 1982; Dubelman *et al.* 1982; Wojeck *et al.* 1983). The role of protective clothing in reducing exposure has also been evaluated by some investigators (Franklin *et al.* 1982; Putnam *et al.* 1983).

Over 17 million kilograms of herbicides are applied annually during the months of May and June to control various broadleaved and grassy weeds in crops on the Canadian plains (source: 1984 Herbicide Use Survey, Manitoba Department of Agriculture). More than 90% of these chemicals are applied by tractor-drawn ground-rigs. In 1981, a study was initiated to quantify potential exposure to and absorption of the dimethylamine salt of 2,4-D [(2,4-dichlorophenoxy)acetic acid] by farmers under Canadian field conditions. The objectives were to: (1) estimate the magnitude of overall potential dermal and inhalation exposure of farmers; (2) measure, 2,4-D excretion in the urine as an indicator of absorption; (3) determine the relative importance of the inhalation and dermal (including hands) routes of exposure, and (4) evaluate possible correlations between estimates of exposure and absorption with operational and environmental factors.

Materials and Methods

Field Procedures

Study Group: Seven male, caucasian farmers who sprayed their own fields with the dimethylamine salt of 2,4-D (2,4-D DMA), using ground-rigs, participated in the study. Four subjects took part during 1981 and five in 1982, with two participating in both years; all lived within a 15 km radius of Regina, Saskatchewan, Canada. They were from 24 to 57 years of age, with the body weight, height, and calculated body surface area varying respectively from 65 to 93 kg, 164 to 196 cm, and 18,040 to 21,520 cm^2. Five of the subjects were right-handed, one left-handed, and one ambidextrous.

Control Group: Eight volunteers, who were not involved in the spray operations, participated as controls, four in 1981 and four in 1982. They provided urine samples starting before the spray season and continuing throughout the experimental period in order to correct for background levels (Grover *et al.* 1985).

Spray Operation: All spray operations were conducted from mid-June to early July. All subjects followed their normal mixing and spraying procedures. A laundered set of standardized work clothing was provided to each subject prior to each spraying operation. One subject wore protective gloves but none used respirators. The tractor-drawn ground-rigs consisted of trailer-mounted spray tanks equipped with booms at the rear, with pumps powered by tractor power take-offs. The tank capacity and the boom size varied from 680 to 2,270 L and 12 to 24 m, respectively. Some of the tractors had cabs. The height of the spray booms above the target varied from 34 to 76 cm, depending on the nozzle type and spray pressure.

The participants sprayed 2,4-D DMA (water-soluble formulation) at rates of 315 to 630 g/ha acid equivalent (a.e.) and in spray volumes varying from 45 to 123 L/ha. The spray pressure varied from 172 to 310 kPa. The number of times a participant filled the tank during a single spray operation varied from one to 11 times, depending on the hectarage sprayed. A single spray operation was defined as an uninterrupted work period which included transferring, mixing, and spraying of the herbicide as well as breaks for rest and meals. When spray operations were stopped due to poor weather conditions, mechanical breakdown or other reasons, the resumption of spraying was then considered a second spray operation for which a clean set of standardized clothing, and dermal and air samplers were provided. Each completed spray operation was considered an "exposure" with pertinent data collection and sampling. Most of the participants undertook several spray operations in a given season: this number varied from one to seven spray operations per farmer spread over 1 to 17 days and thus single spray operations were not always consecutive. The hectarage and total amount of 2,4-D DMA sprayed per operation varied from 16 to 194 ha and 6.7 to 88.3 kg (a.e.), and spray operations lasted from 55 to 870 min.

Clothing: A standardized set of laundered clothing was issued to all subjects at the start of each spray operation. Each set consisted of cotton work pants, a short-sleeved, cotton T-shirt, and long-sleeved, cotton coverall of heavy material. Thus, most of the body was covered by two layers of clothing, leaving the neck and hands exposed, while the head was partially covered by an open-mesh baseball cap. At the end of each exposure, the clothing was collected and samplers were removed and stored.

Sampling Procedures

Air: A polyurethane foam (PUF) plug, 20 mm in diameter by 50 mm in length contained in a Pyrex glass holder (Grover and Kerr

1981), was attached to the chest on the outside of the coverall. The holder was held with the air inlet facing down within the breathing zone of each subject (Figure 1). The air was sampled at 2.0 L/min using a portable pump (Spectrex model PAS-3000) for the entire spray operation. After each operation, the glass holder containing the foam plug was labelled, transferred to a polyethylene bag, and stored at −10°C until extraction.

Patches: During each spray operation, 2,4-D deposition was determined by a patch method (Franklin *et al.* 1981, 1982). Glass fiber filters, 47 mm in diameter (AP40 microfiber glass discs, Millipore), were impregnated with 0.6 mL of ethylene glycol, using a micropipette. The filters were mounted in a sandwich of coarse surgical gauze backed by a piece of cardboard to protect them from mechanical damage and to reduce accidental loss. The surgical gauze was rinsed with methanol and dried before use. Nine patches were located under the work clothing: one on the left side of the chest anteriorly, and on each upper arm, wrist, knee, and ankle (Figure 1). An additional four patches were placed over the clothing (Figure 1). Two of these were located at the neck and near the left elbow respectively. The other two were mounted on petri-dishes (Millipore PD15 04700) and attached on the left side of the head on the cap, and on the left side of the chest. After each spray operation, the glass fiber patches were collected, transferred to screw-cap vials, and stored at −10°C until extraction.

Hands: After each spray operation, the applicator's hands were rinsed in 750 mL of 1% $NaHCO_3$ solution, which was then transferred to a polyethylene bottle and stored at −10°C until analysis.

Urine: Composite 24-hr urine samples were collected beginning 1 day before the first spray operation and then continuously throughout succeeding operations and up to 7 days after the last spray operation. All urine voids for each 24-hr period were collected in disposable polyethylene-lined, 2.5-L urine specimen storage containers (Fisher Scientific, Cat. No. 14-375-119). Each day, containers were collected, marked with the name of the subject and the date, and stored at −10°C until extraction.

Fig. 1. Subject showing the location of samplers under (left) and over (right) the protective clothing

Analytical Methods

Extraction, Clean-up and Methylation

(a) *Foam plugs, Sampling patches and Hand washes:* The PUF plugs, sampling patches and hand washes were solvent extracted, and the extracts methylated with diazomethane prior to Florisil® column clean-up and gas chromatographic analysis, using the procedures described by Grover *et al.* (1985).

(b) *Urine:* The urine samples were thawed at room temperature and shaken to suspend any sediments prior to sub-sampling. The total volume of the urine sample was measured and a 100-mL aliquot was analyzed for 2,4-D residues by the modified procedure of Smith and Hayden, 1979 (Grover *et al.* 1985).

Gas Chromatography: A Tracor Model 560 gas chromatograph, equipped with a ^{63}Ni linearized electron-capture detector was used with a Varian Model 8000 autosampler and Vista 401 data system. A 1.83 m × 4 mm i.d. coiled glass column packed with 100–200 mesh Ultrabond (RFR Corp, Hope, RI) gave a 2.7 min retention time for 2,4-D methyl ester under the following operating conditions: 95% argon-methane (carrier gas, 40 mL/min; purge gas, 20 mL/min); column 180°C; injector 220°C; detector 350°C.

Calculations

Residue data from air and patch samplers, as well as hand wash solutions, were obtained for a total of 30 separate spray operations during 1981/82. These data were used to calculate the total potential inhalation and dermal doses for each spray operation.

Inhalation Exposure: The airborne concentration ($\mu g/m^3$) of 2,4-D (a.e.) in the breathing zone during each spray operation was calculated from the amount (μg) of 2,4-D (a.e.) on the PUF plug, the air sampling time (min), and the air sampling rate (L/min). Assuming a medium level of activity with a theoretical inhalation volume of 1.74 m^3/hr (Spector 1956), and knowing the individual body weight (kg) and time (hr) exposed, the total amount (μg) of 2,4-D (a.e.) assumed to have been inhaled, and the inhaled dose normalized for body weight (ng/kgBW) and the amount of 2,4-D (a.e.) applied [ng/kgBW/kg 2,4-D (a.e.) applied] were calculated.

Dermal Exposure: (a) *Dermal samplers:* The total body surface area for each subject was calculated, using the formula:

$$\text{Surface Area} = 0.007184(BW)^{0.425} \times (ht)^{0.725}$$

where the body weight (BW) is expressed in kilograms and the body height (ht) in meters (Dubois and Dubois 1916). The surface areas of the various body regions were calculated by the anatomic proportions estimated by Spear *et al.* (1977).

The potential 2,4-D DMA (a.e.) dermal doses (μg) for the various regions of the body were determined from sampling patch analysis (μg/cm^2) and the regional body surface areas (cm^2) (Table 1). These values were summed to estimate total potential dermal deposition (μg) and also normalized as described under inhalation exposure.

(b) *Hand wash:* Exposure to the hands for each spray operation was calculated using the concentration (μg/mL) of 2,4-D (a.e.) in the hand wash solution and the hand wash volume (750 mL). The dose and normalized dose was calculated as above.

Urinary Excretion: The total amount (μg) of 2,4-D (a.e.) excreted per subject per day was readily calculated from the urine volume (mL) and the concentration (μg/mL) of 2,4-D (a.e.) in each 24-hr void. The urine collections for the 30 individual spray operations resulted in nine cumulative urine samples, which were also normalized.

Statistical Analysis: Despite measures taken to prevent accidental loss or destruction of sampling patches, a few were lost during spray operations. In order to estimate these missing values, tests of normality were carried out by the method of Shapiro and Wilks (1965). Since these tests indicated that the sampling patch residue data followed a log normal distribution for each of the body locations, estimation of missing values was possible by a correlation program (SRS S009), using the LOG Y(I) transforms of the data. The method of Anscombe and Tukey (1963) was used to establish whether there were any outliers in the patch data.

Simple regression analysis was used to determine whether significant correlations existed between various operational and environmental parameters and inhalation exposure, dermal exposure (with and without hands), and urinary excretion.

Results and Discussion

Estimation of Potential Exposure

Inhalation Exposure: The volumes of air sampled during 30 spray operations ranged from 0.1 to 1.7 m^3, with a median volume of 0.5 m^3 (Table 2), for sampling durations of 55 min to 14.5 hr per spray operation. The median airborne residue concentration was 2.1 μg/m^3, with a range of <0.01 to 101 μg/m^3, which were similar in magnitude to those reported by WHO (1984). Although 13 of 30 exposures were carried out with tractors equipped with varying kinds of enclosures or 'cabs', no significant differences in airborne residues were observed between the two groups. This may have been due to the wide range in concentration of the herbicide in the air and the variation in protection provided by cabs. Wojeck *et al.* (1983) reported an 85% reduction in total applicator exposure to the herbicide paraquat when two similar tractors were compared, with one being 'open' and the other equipped with an air-conditioned 'cab'. Assuming a medium activity level, the median amount of 2,4-D (a.e.) inhaled and the median inhalation dose per spray operation were estimated to be 13.7 μg (range <1 to 324) and 202 ng/kgBW (range <1 to 3,680), respectively (Table 2). Inhalation exposure was not significantly correlated with any of the other usual activities associated with the spray operations, *e.g.*, the amount of 2,4-D applied, or with the prevailing weather conditions, *e.g.*, wind speed during spraying, *etc.*

Dermal Exposure: (a) *Total body (minus the hands):* All sampling patches, including those located under the garments, contained detectable levels of 2,4-D, indicating that the herbicide had penetrated through the clothing on all regions of the body. The deposit estimates of 2,4-D (a.e.) on various regions of the body ranged from 2 ng/cm^2 to 1,481 μg/cm^2, with three statistically established outliers. When these values were not taken into consideration, the dermal 2,4-D (a.e.) deposit data for the whole body (minus the hands) calculated from 30 single spray operations, gave a median dermal dose per spray operation of 27.9 μg/kgBW, with a minimum of 7.5 μg/kgBW and a maximum of 278 μg/kgBW (Table 3).

There was no significant correlation between operational and environmental parameters and total calculated dermal exposure (with hands), which probably reflects the masking of the dermal exposure to the rest of the body by the large but irregular exposure to the hands. However, if the hand exposure is not taken into account, then the log transform of the total dermal deposits (exposure estimates) was significantly correlated with 1) area sprayed per exposure, $r = 0.793$ (Figure 2A); 2) duration of exposure, $r = 0.788$ (Figure 2B); 3) amount of 2,4-D applied, $r = 0.836$ (Figure 2C), and 4) most strongly with the number of tank fills per exposure, $r = 0.886$ (Figure 2D). All of these operational activities are correlated amongst themselves.

(b) *Hands:* Analyses of the 30 individual hand wash samples indicated a median 2,4-D (a.e.) dermal dose per spray operation of 120 μg/kgBW and a range of 0.1 to 552 μg/kgBW (Table 3). High deposits on the hands have also been reported by several other investigators (Dubelman *et al.* 1982; Draper and Street 1982; Wojeck *et al.* 1983). There were no significant correlations between operational and environmental parameters examined in this study and the extent of hand exposure.

Table 1. Dermal patch location, the region of the body represented by the patch, and the percent of the total body surface area represented by each body region

Location of patch	Body regions represented	Surface area[a] (% of total)
Head	Head	5.60
Neck	Neck	1.20
Elbow (l,r)	Upper arm (l,r)	2 × 4.85 = 9.70
Wrist (l,r)	Forearm (l,r)	2 × 3.35 = 6.70
Chest	Chest, back, shoulders	22.80
Knee (l,r)	Thigh (l,r), hip (l,r)	2 × 13.55 = 27.10
Ankle (l,r)	Calf (l,r), foot (l,r)	2 × 9.95 = 19.90
Hand (l,r)[b]	Hand (l,r)	2 × 3.50 = 7.00

[a] Based on anatomic proportions estimated by Spear *et al.* (1977)
[b] Potential exposure on hands was determined by hand washes

Table 2. Calculated amount of 2,4-D (a.e.) available for inhalation, and the calculated inhalation dose of ground applicators spraying 2,4-D DMA

	Volume of air sampled (m^3)	Airborne concentration ($\mu g/m^3$)	Calculated amount inhaled[a] (μg)	Calculated inhaled dose[a] (ng/kgBW)[b]
Median	0.5	2.1	13.7	202
Range	0.1–1.7	<0.01–101	<1–324	<1–3,680

[a] Estimate based on medium activity level (1.74 m^3/hr inhaled) and time exposed (hr)
[b] Nanograms per kilogram of body weight

Table 3. Median, minimum, and maximum values for dermal deposits from 30 single exposures by ground applicators using 2,4-D DMA

Body region	Mean surface area (cm^2)	Dermal deposit estimates from single exposures (μg/kgBW)[a] median	minimum	maximum
Whole body (minus the hands)	18,425	27.9	7.5	278
Hands	1,366	120	0.1	552

[a] Micrograms per kilogram of body weight

Exposure Based on Urinary Excretion

The cumulative amounts of 2,4-D (a.e.) excreted per subject ranged from 467 to 6,324 μg, with a median value of 1,523 μg (Table 4). These values, when normalized for body weight, resulted in a range of 6.6 to 77.1 μg/kgBW and a median value of 16.4 μg/kgBW. In all subjects participating in the study, detectable levels of 2,4-D (a.e.) were still present in urine samples collected four to seven days after the last exposure. Other investigators (Draper and Street 1982; Franklin *et al.* 1982; Nash *et al.* 1982; Åkerblom *et al.* 1983; Libich *et al.* 1984) also observed urinary excretion of phenoxy herbicides a few days after the last field exposure. The urinary 2,4-D levels decreased to background amounts in only one subject [B(81)], and this occurred 8 days after the first exposure. In this case, there was an interval of 13 days between the first and second spray operations. Thus, the values (Table 4) for total 2,4-D (a.e.) excreted per subject (μg or μg/kgBW) represent an underestimation of total urinary 2,4-D (a.e.) excretion.

Regression analyses were carried out with only 7 of the 9 subjects, because 2 subjects had extreme urinary excretion values (subjects C(81) and F(81); Table 4). The total urine excretion value of subject C(81) was high because, unknown to the authors, the subject had sprayed 2,4-D extensively just prior to the commencement of this study and, as a result, his background level in urine was about 860 ng/mL 2,4-D (a.e.). In contrast, the urinary excretion of subject F(81) was low relative to his large dermal exposure (Table 5), and for no apparent reason. Simple regression analyses indicated very significant correlations between the total cumulative

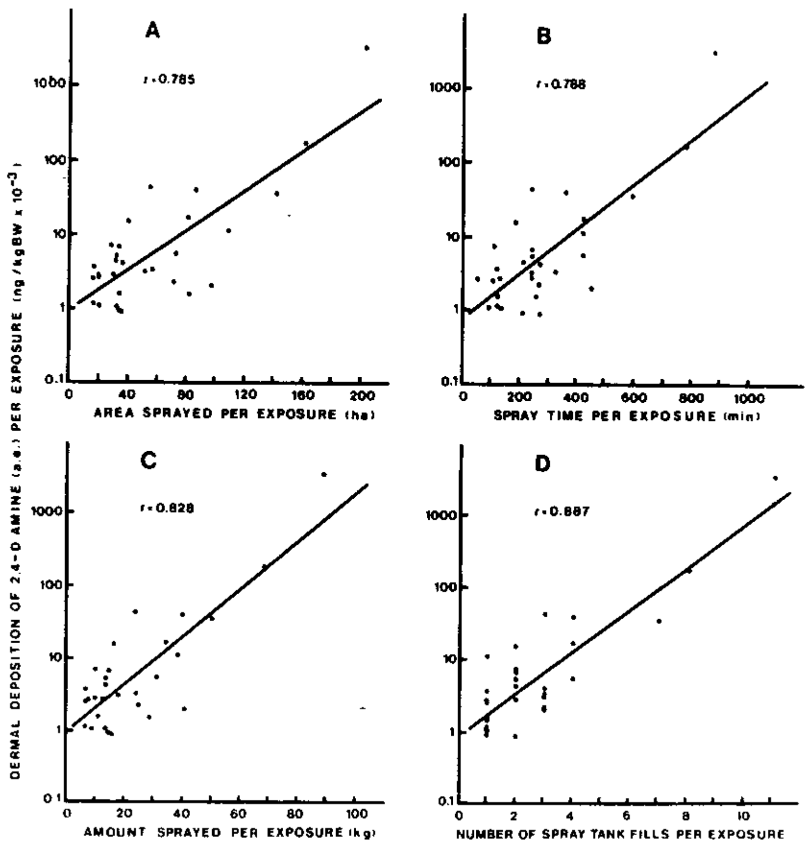

Fig. 2. The relationships between area sprayed (A), spray time (B), amount applied (C), number of tank fills (D) and dermal deposition (minus hands) of 2,4-D DMA (a.e.) per exposure

Table 4. Estimates of total 2,4-D (a.e.) excreted per subject

Subject	Number of exposures	Estimates of 2,4-D acid (a.e.) (μg)	(μg/kgBW)[b]	(μg/kgBW/ exposure)
C(81)[a]	1	5,250	56.6	56.6
B(82)	2	820	9.8	4.9
C(82)	2	1,520	16.4	8.2
F(81)	2	470	7.2	3.6
A(82)	3	1,900	22.6	7.5
B(81)	3	560	6.6	2.2
D(82)	4	1,660	18.8	4.7
G(82)	6	6,320	77.1	12.9
E(81)	7	1,050	15.4	2.2

[a] The subject had sprayed extensively prior to the commencement of the study

[b] Micrograms per kilogram of body weight

amount of 2,4-D (a.e.) excreted in the urine per subject and a) cumulative area sprayed, r = 0.895 (Figure 3A); b) cumulative spray time, r = 0.929 (Figure 3B); c) cumulative amount applied, r = 0.903 (Figure 3C); and d) cumulative number of tank fills, r = 0.913 (Figure 3D). As noted earlier, all four of these operational parameters are also correlated amongst themselves. Finally, it is of interest to note that no correlation (r = 0.3) existed between the total 2,4-D (a.e.) excreted and the total calculated dermal exposure (patches plus hands). This is in agreement with the results of Lavy *et al.* (1980b) and Nigg and Stamper (1983), who studied the exposure of forestry applicators to 2,4,5-T and airboat handgun applicators' exposure to 2,4-D, respectively. They observed little or no correlation between the total amount of phenoxy herbicide excreted and the total estimated dermal exposure.

Relative Exposure Estimates

The cumulative estimates of potential inhalation, dermal and hand exposures, normalized for both body weight (kgBW) and the amount of 2,4-D applied (kg a.e.), were calculated by summing all spray operations for each subject (Table 5). These values were, in turn, summed to give the total cumulative potential exposure for each subject. The total 2,4-D urinary excretion was calculated by summing the amounts of 2,4-D (a.e.) found in all 24-hr urine voids for each subject, and then normalizing as above.

One of the objectives of the present study was to

Table 5. Cumulative estimates of inhalation, dermal, hand, and total exposure and total urinary 2,4-D (a.e.) excretion per subject and fractional contributions for the various exposure routes

Subject and year of study	Body wt. (kg)	Amount of 2,4-D applied (kg a.e.)	No. of spray operations	Cumulative potential exposures (ng/kgBW/kg a.e.)[a]				Total urinary excretion	Fractional contribution (% of calculated exposure)			Fraction of total exposure
				inhalation	dermal	hand	total		inhalation	dermal	hands	urinary
A(82)	84	68.4	3	5	1,740	13,100	14,800	220	0.1	11.7	88.2	1.5
B(81)	84	60.1	3	8	4,520	18,300	22,800	110	0.1	19.8	80.2	0.5
B(82)	84	49.3	2	14	3,670	36,800	40,500	199	0.1	9.0	90.9	0.5
C(81)[b]	93	23.9	1	1	1,010	4,970	5,980	2,360	0.1	16.9	83.1	39.5
C(82)[c]	93	22.7	2	93	3,940	1,730	5,760	721	1.6	68.3	30.1	12.5
D(82)	88	89.9	4	435	15,200	66,600	82,300	210	0.5	18.5	80.9	0.3
E(81)	68	71.3	7	115	19,100	105,000	124,000	216	0.1	15.4	84.5	0.2
F(81)	65	127.9	2	5	301,000[d]	40,300	341,000	56	0.1	88.2	11.8	0.1
G(82)	82	186.0	6	277	57,900	49,600	108,000	414	0.3	53.7	46.0	0.4
Median	84	68.4	3	14	5,420	36,800	40,500	216	0.1	18.5	80.9	0.5

[a] Nanograms per kilogram of body weight per kilogram acid equivalent
[b] Subject sprayed extensively prior to experimental sampling
[c] Subject used protective gloves
[d] Includes large amount in one head patch

determine the relative importance of the inhalation, dermal (total body minus the hands), and hand routes of exposure. In each of the nine cumulative exposures (Table 5), the data indicate that exposure by inhalation was less than 2% of the total exposure, and that the hands were the area of the body receiving the greatest deposition. In six of the cumulative exposures, exposure to the hands accounted for 80 to 90% of the total amount deposited. Although relative hand exposures were much smaller in some cases, this can be explained by the fact that a very large amount of 2,4-D (a.e.) was found on one head patch of Subject F(81), and that Subject C(82) wore protective gloves. Because of the relatively large exposure to the hands, the use of protective gloves by the other subjects would probably have reduced their dermal exposure. Thus, exposure to the rest of the body was in the order of 10 to 20% of the total cumulative potential exposure. However, the relative cumulative potential exposures for the inhalation, dermal (minus the hands), and hand routes of exposure are not indicative of the contributions of each exposure route to the total amount of 2,4-D which entered the body. Widely differing regional variations in percutaneous penetration in man have been observed by Maibach *et al.* (1971) using radiolabelled pesticides. In addition, when percutaneous absorption of 2,4-D DMA dissolved in water was studied in monkeys (unpublished data), pronounced differences were observed in the percentage of the applied dose excreted when the chemical was applied to the forearm (6%) and to the forehead (31%), respectively.

Total 2,4-D urinary excretion was less than 2% of

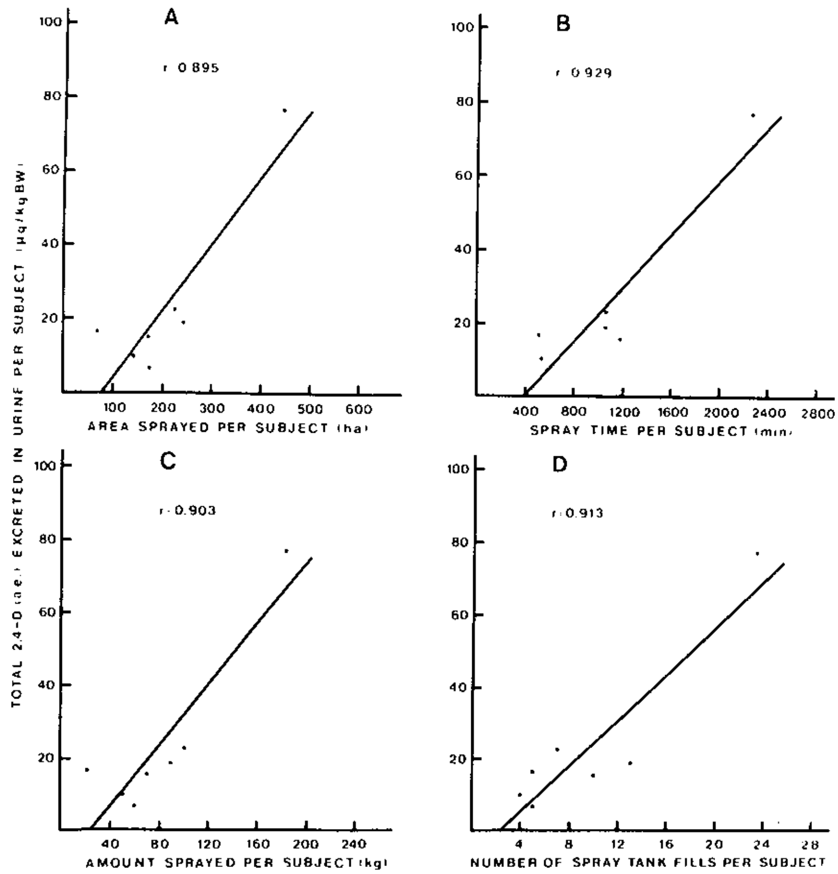

Fig. 3. The relationships between cumulative area sprayed (A), cumulative spray time (B), cumulative amount applied (C), cumulative number of tank fills (D) and total 2,4-D (a.e.) excreted in urine per subject

the total cumulative potential exposure for 7 of the 9 cumulative exposures (Table 5). Urinary excretion, as a percent of the total cumulative potential exposure, was much greater for subject C who used protective gloves in 1982, and who, in 1981, sprayed 2,4-D formulations extensively prior to the experimental sampling. Although in both years Subject C effectively increased his urinary excretion relative to his total exposure, the reasons for this differed in the two years, illustrating how urinary excretion values may be affected by different factors.

In summary, inhalation and dermal exposures and the urinary 2,4-D (a.e.) excretion of farmers using tractor-drawn ground-rigs for 30 separate spray operations with 2,4-D DMA were measured. The hands received most of the 2,4-D (a.e.) deposited on the body (80 to 90% of the total cumulative potential exposure). The calculated dermal deposition on the rest of the body was 10 to 20% of the total cumulative potential exposure, whereas the calculated amount available for inhalation was less than 1% in most cases. Less than 2% of the calculated cumulative potential exposure was excreted in the urine.

Safety, Predictability of Exposure, and Hazard Assessment

These results, which show that most of the deposition occurs on the hands, have important implications when recommending protective measures to reduce exposure, and also for theoretical exposure modelling. It is apparent that deposition on the hands is influenced by working habits, and is not readily predictable or reliably related to the environmental or operational conditions measured. Thus, it would be prudent to recommend in similar work situations that methods to reduce hand exposure be introduced to minimize exposure. However, the effectiveness of measures suggested to reduce hand exposure (impermeable gloves, closed transfer systems etc.) need additional evaluation (Henry 1985).

If hand exposure can be prevented, then contact with other areas of the body can be related to operational parameters such as the area, time, and amount of chemical sprayed, and the number of tank-fills. This predictability is useful where estimates of contact exposure are necessary. By comparison, only marginal reductions in total exposure are likely to be achieved by additional pieces of protective equipment other than coveralls.

One of the reasons for conducting this study was to determine whether the amount of 2,4-D (a.e.) absorbed by Canadian prairie farmers during their annual herbicide spray program was of toxicologic concern. The most appropriate exposure measurements for such considerations are the daily and total amounts of 2,4-D (a.e.) excreted in the urine, because these provide an indirect measure of the minimum amount of chemical which entered the body and which could have exerted a toxicologic effect. However, urinary 2,4-D excretion represented an underestimation of exposure, because it did not take into account either 2,4-D excretion with the feces, or residues remaining in the body at the end of the period of urine collection; although, based on two studies with humans ingesting small doses of 2,4-D acid, both of these are unlikely to exceed 20–25% of the amounts excreted in the urine (Kohli *et al.* 1974; Sauerhoff *et al.* 1977). In addition, the subjects washed their hands and removed the contaminated standardized clothing immediately after each spray operation and this practice may not be representative of the majority of farmers.

The present study indicated that the total amounts of 2,4-D (a.e.) excreted in the urine of farmers applying 2,4-D amine salts ranged from 6.6 to 77.1 μg/kgBW (Table 4). The greatest amount excreted on an exposure basis was 12.9 μg/kgBW (Table 4) if the value for subject C(81), which was inflated because this subject had sprayed 2,4-D extensively immediately prior to the commencement of this study, is ignored. The amount can be compared to single doses of between 5 and 36 mg 2,4-D (a.e.)/kgBW which were reported to have no acute adverse effects in adult humans (Apffel 1959; Kohli *et al.* 1974; Saueroff *et al.* 1977; Seabury 1963), in order to estimate a Margin of Safety (MOS) for acute toxic effects. On this basis, one arrives at MOS values of between 388 and 2790; in general a MOS value of 10 is considered adequate if it is based on acute toxicity tests in humans, as is the case with 2,4-D. Thus, even taking into consideration that the urinary 2,4-D acid excretion values may represent a 20–25% underestimation of exposure, no acute toxic effects are likely to result from ground spray operations such as those typical of the present study; that is, using normal operating procedures and a double layer of clothing.

Whether such 2,4-D herbicide user exposures might have adverse long-term effects remains open to question. Neither a firm No Observed Effect Level for chronic exposure nor the carcinogenic potential of 2,4-D acid or its amine salts or esters have been established in laboratory animals or humans (*WHO* 1984). Furthermore, 2,4-D is often used mixed with other herbicides, which might increase its toxicity. Moreover, some epidemiologic studies on workers occupationally exposed to chlorophenoxy herbicides during the manufacture or use of these chemicals or their chlorophenol precursors have indicated an increased risk of certain cancers; other studies were inconclusive (Axelson *et al.* 1980; Hardell 1981; Hardell *et al.* 1981; *IARC* 1983; Lynge 1984). These uncertainties call for continued caution in the use and handling of 2,4-D and other chlorophenoxy herbicides.

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