

8. SELECTED BIRTH DEFECTS AND DEVELOPMENTAL DISABILITIES

8.1 Introduction

Twelve selected birth defects and 4 developmental disabilities, defined by ICD-9-CM code in Table 8-1, have been suggested as possibly dioxin-related [14] or have been the focus of veteran and public interest.

In this section, rates are expressed per 1000 children.

Table 8-1

ICD Definitions of Twelve Selected Birth Defects and Four Developmental Disabilities

a) Birth Defects

Name	ICD Codes
Anencephaly	740.0
Spina bifida	741.0 741.9
Hydrocephalus	742.3
Cleft Palate	749.0
Cleft lip/palate	749.1 749.2
Esophageal atresia	750.3
Anorectal atresia	751.2
Hypospadias	752.6
Congenital hip dislocation	754.3
Polydactyly	755.0
Limb reduction deformities	755.2 755.3 755.4
Down's syndrome	758.0

b) Developmental Disabilities

Name	ICD Codes
Disturbance of emotion specific to childhood and adolescence	313
Hyperkinetic syndrome of childhood	314
Specific Delays in Development	315
Mental Retardation	317 318 319

Counts of these 16 selected anomalies among all pre-SEA (n=4145) and post-SEA (n=2647) Ranch Hand and Comparison children and among all pre-SEA (n=2742) and post-SEA (n=1772) children whose father is a Ranch Hand or Comparison who satisfies the conditions of Models 1, 2 and 3 are shown in Table 8-2.

Table 8-2

Counts of 12 Selected Birth Defects and 4 Developmental Disabilities
in Pre-SEA and Post-SEA Ranch Hand and Comparison Children
By the Fathers Inclusion in Models 1, 2 or 3

a) Birth Defects				
Name	All		Models 1,2,3	
	Pre-SEA	Post-SEA	Pre-SEA	Post-SEA
Anencephaly	1	1	1	1
Spina bifida	3	3	3	3
Hydrocephalus	5	1	5	1
Cleft Palate	6	6	6	4
Cleft lip/palate	7	5	7	4
Esophageal atresia	2	2	0	1
Anorectal atresia	2	1	1	1
Polydactyly	3	1	3	1
Limb reduction deformities	2	4	1	4
Hypospadias	4	15	3	10
Congenital hip dislocation	8	25	8	14
Down's syndrome	4	11	2	7

b) Developmental Disabilities				
Name	All		Models 1,2,3	
	Pre-SEA	Post-SEA	Pre-SEA	Post-SEA
Disturbance of emotion specific to childhood and adolescence	11	18	9	10
Hyperkinetic syndrome of childhood	54	77	39	62
Specific Delays in Development	103	179	73	142
Mental Retardation	12	13	10	7

Occurrences of these selected anomalies among pre-SEA and post-SEA Ranch Hand children by exposure restriction (D>10 ppt, D>5 ppt) are shown in Table 8-3 for those children who enter a Model 1 or Model 2 analysis.

Table 8-3

**Occurrences of Selected Anomalies in Ranch Hand
Children Who Enter a Model 1 or Model 2 Analysis**

Name	Exposure Restriction	n	Counts by Time of Conception and the Father's Initial Dioxin						
			Low	Pre-SEA			Low	Post-SEA	
				Medium	High	n		Medium	High
Anencephaly/ Ancephalus	D>10 ppt	700	0	0	0	508	0	1	0
	D>5 ppt	1058	1	0	0	690	0	1	0
Spina Bifida	D>10 ppt	700	1	0	0	508	1	1	1
	D>5 ppt	1058	0	1	0	690	0	1	2
Hydrocephalus	D>10 ppt	700	1	0	0	508	0	0	0
	D>5 ppt	1058	0	2	0	690	0	0	0
Cleft Palate	D>10 ppt	700	1	1	1	508	0	0	0
	D>5 ppt	1058	0	2	1	690	0	0	0
Cleft Lip/palate	D>10 ppt	700	1	1	0	508	0	1	0
	D>5 ppt	1058	1	2	0	690	0	1	1
Esophageal atresia	D>10 ppt	700	0	0	0	508	1	0	0
	D>5 ppt	1058	0	0	0	690	0	1	0
Anorectal atresia	D>10 ppt	700	0	0	0	508	0	0	1
	D>5 ppt	1058	0	0	0	690	0	0	1
Polydactyly	D>10 ppt	700	0	0	0	508	0	1	0
	D>5 ppt	1058	1	0	0	690	0	0	1
Limb reduction deformities	D>10 ppt	700	0	1	0	508	1	0	0
	D>5 ppt	1058	0	1	0	690	0	1	0
Hypospadias	D>10 ppt	700	0	0	0	508	0	4	0
	D>5 ppt	1058	1	0	0	690	0	4	0
Congenital Hip Dislocation	D>10 ppt	700	0	2	1	508	0	2	1
	D>5 ppt	1058	0	2	2	690	1	2	1
Down's Syndrome	D>10 ppt	700	0	1	0	508	0	0	1
	D>5 ppt	1058	0	1	0	690	1	0	1

Table 8-3 (Continued)

b) Developmental Disabilities

Name	Exposure Restriction	n	Counts by Time of Conception and the Father's Initial Dioxin						
			Pre-SEA			Post-SEA			
			Low	Medium	High	n	Low	Medium	High
Emotional Disturbance	D>10 ppt	700	1	1	1	508	0	3	0
	D>5 ppt	1058	1	2	1	690	1	2	1
Hyperkinetic Syndrome	D>10 ppt	700	5	6	0	508	3	7	6
	D>5 ppt	1058	2	11	0	690	10	8	10
Delays in Development	D>10 ppt	700	4	9	6	508	12	25	10
	D>5 ppt	1058	5	14	6	690	13	29	18
Mental Retardation	D>10 ppt	700	0	1	0	508	0	1	1
	D>5 ppt	1058	0	2	0	690	1	1	1

8.2 Pre-post SEA Exposure Analyses

Only delays in development and hyperkinetic syndrome can be analyzed for an association with dioxin because the counts of abnormalities in the other 14 categories are too small to permit statistical analysis. Analyses using Models 1, 2 and 3 were carried out to determine whether any of the pre-SEA to post-SEA changes in delays in development or hyperkinetics syndrome odds ratios were related to the father's dioxin body burden without adjustment for covariates. The results from all children and full sibling children are shown in tables 8-4 through 8-15.

Specific Delays in Development (All Children)

Model 1: Children of Ranch Hands - $\log_2(\text{Initial Dioxin})$

Without adjustment for covariates (Table 8-4 [a]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.035$). This significance is due to a reversal in the pattern of the rates of delays in development with time of conception. The delays in development rate increases with initial dioxin in pre-SEA children while the rate decreases with initial dioxin in post-SEA children.

Without adjustment for covariates (Table 8-4 [b]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.044$). This significance is due to a difference in the pattern of rates of delays in development with time of conception. The rate increases with initial dioxin in pre-SEA children while the rate is constant with respect to initial dioxin post-SEA children.

Table 8-4

Pre-Post SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
 Restrictions: All Children of Ranch Hands
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted									
Exposure Restriction	Initial Dioxin	n	Time of Conception Relative to the Father's Duty in SEA			n	Post-SEA		p-Value
			Pre-SEA Abn	Rate	Abn		Rate		
a) $D > 10$ ppt ($n=1208$)	Low	249	4	16.1	106	12	113.2	0.035	
	Medium	338	9	26.6	245	25	102.0		
	High	113	6	53.1	157	10	63.7		
b) $D > 5$ ppt ($n=1748$)	Low	286	5	17.5	155	13	83.9	0.044	
	Medium	616	14	22.7	308	29	94.2		
	High	156	6	38.5	227	18	79.3		

Specific Delays of Development (All Children)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-5 [a]), there is borderline significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception in children of Ranch Hands having more than 10 ppt current dioxin ($p=0.074$). This significance is due to the inconsistent pattern in the rates of delays in development across levels of current dioxin, time since tour and time of conception. The finding is caused by the changing pre-SEA patterns which, of course, have no relationship with the father's subsequent dioxin exposure.

Without adjustment for covariates (Table 8-5 [b]), there is significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.032$). This significance is due to the inconsistent pattern of the delays in development rates across levels of dioxin, time since tour and time of conception. Like the corresponding finding in Table 8-5 [a], this finding is caused by the changing pre-SEA patterns which have no relationship with the father's subsequent dioxin exposure.

Table 8-5

Pre-Post SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
 Restrictions: All Children of Ranch Hands
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 2: $\text{Log}_2(\text{Current Dioxin})$, Time

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤18.6	14.6 (2/137)	27.3 (5/183)	108.1 (4/37)	0.074
		>18.6	21.1 (2/95)	23.4 (4/171)	25.6 (2/78)	
	Post-SEA	≤18.6	96.8 (6/62)	104.5 (14/134)	55.6 (4/72)	
		>18.6	100.0 (4/40)	111.1 (12/108)	75.3 (7/93)	
b) D>5 ppt	Pre-SEA	≤18.6	6.4 (1/157)	28.8 (9/313)	60.6 (4/66)	0.032
		>18.6	20.0 (3/150)	22.2 (6/270)	19.6 (2/102)	
	Post-SEA	≤18.6	88.9 (8/90)	103.4 (18/174)	72.7 (8/110)	
		>18.6	47.6 (3/63)	110.3 (15/136)	68.4 (8/117)	

Specific Delays in Development (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-6), there is no significant overall variation in the association between specific delays in development and categorized current dioxin with time of conception ($p=0.664$). Furthermore the association between specific delays in development and time of conception among children of Ranch Hands in the High ($p=0.471$), Low ($p=0.374$) and Unknown ($p=0.937$) categories are not significantly different from the corresponding association among children of Comparisons in the Background category.

Table 8-6

Pre-Post SEA Counts and Rates of Specific Delays in Development

Variable: Specific Delays in Development
 Restrictions: All Children of Ranch Hands and Comparisons
 Category: Time of Conception Relative to the Father's Duty in SEA
 Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted									
Time of Conception Relative to the Father's Duty in SEA									
Exposure Category	n	Pre-SEA		Post-SEA			Odds Ratio	Category Contract	p-Value
		Abn	Rate	n	Abn	Rate			
Background	1459	37	25.4	981	71	72.4	3.00	All Exp Categ	0.664
Unknown	582	17	29.2	282	24	85.1	3.09	Unk vs Bkgd	0.937
Low	290	8	27.6	174	20	114.9	4.58	Low vs Bkgd	0.374
High	168	6	35.7	227	16	70.5	2.05	High vs Bkgd	0.471

Specific Delays in Development (Full Siblings)

Model 1: Children of Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$

Without adjustment for covariates (Table 8-7 [a]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.045$). This significance is due to a reversal in the pattern of rates of delays in development with time of conception. The delays in development rate increases with initial dioxin in pre-SEA children while the rate decreases with initial dioxin in post-SEA children.

Without adjustment for covariates (Table 8-7 [b]), there is significant variation in the association between specific delays in development and initial dioxin with time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.053$). This significance is due to a difference in the pattern of rates of delays in development with time of conception. The delays in development rates increases with the initial dioxin in pre-SEA children while the rate is constant with initial dioxin in post-SEA children.

Table 8-7

Pre-Post SEA Counts and Rates of Specific Delays in Development

Variable: Specific Delays in Development
 Restrictions: Full Siblings of Ranch Hands
 Category: Time of Conception Relative to the Father's Duty in SEA
 Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted								
		Time of Conception Relative to the Father's Duty in SEA						
Exposure Restriction	Initial Dioxin	n	Pre-SEA		n	Post-SEA		p-Value
			Abn	Rate		Abn	Rate	
a) D>10 ppt (n=1030)	Low	231	4	17.3	78	10	128.2	0.045
	Medium	276	9	32.6	206	21	101.9	
	High	103	6	58.3	136	10	73.5	
b) D>5 ppt (n=1489)	Low	252	5	19.8	114	10	87.7	0.053
	Medium	545	14	25.7	245	23	93.9	
	High	135	6	44.4	198	18	90.9	

Specific Delays of Development (Full Siblings)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-8 [a]), there is borderline significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.070$). This borderline significance is due to the inconsistent pattern of rates of delays in development across levels of dioxin, time since tour, and time of conception. In pre-SEA children, the highest (16.1 per 1000) and the lowest (114.3 per 1000) rates occur in children of fathers who had late tours, but the rates appear constant with respect to dioxin in children of fathers who had early tours.

Without adjustment for covariates (Table 8-8 [b]), there is significant variation in the association between specific delays in development and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.053$). This significance is due to the inconsistent pattern of the delays in development rates in children of fathers who had late tours and in children of fathers who had early tours. In post-SEA children the highest rates occur in children of Ranch Hands with intermediate dioxin levels.

Table 8-8

Pre-Post SEA Counts and Rates of Specific Delays in Development

Variable: Specific Delays in Development
 Restrictions: Full Siblings of Ranch Hands
 Category: Time of Conception Relative to the Father's Duty in SEA
 Model 1: $\text{Log}_2(\text{Current Dioxin})$, Time

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n)			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤18.6	16.1 (2/124)	32.3 (5/155)	114.3 (4/35)	0.070
		>18.6	23.5 (2/85)	28.0 (4/143)	29.0 (2/69)	
	Post-SEA	≤18.6	106.4 (5/47)	113.0 (13/115)	62.5 (4/64)	
		>18.6	107.1 (3/28)	97.8 (9/92)	93.3 (7/75)	

Table 8-8 (Continued)

Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n)			p-Value
			Low	Medium	High	
b) D>5 ppt	Pre-SEA	≤18.6	7.9 (1/126)	32.6 (9/276)	66.7 (4/60)	0.053
		>18.6	20.7 (3/145)	25.3 (6/237)	22.7 (2/88)	
	Post-SEA	≤18.6	84.7 (5/59)	111.1 (16/144)	81.6 (8/98)	
		>18.6	56.6 (3/53)	103.8 (11/106)	82.5 (8/97)	

Specific Delays in Development (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-9), there is no significant overall variation in the association between specific delays in development and categorized current dioxin with time of conception in full siblings (p=0.841). Furthermore the association between specific delays in development and time of conception among children of Ranch Hands in the High (p=0.475), Low (p=0.670) and Unknown (p=0.905) categories are not significantly different from the corresponding associations among children of Comparisons in the Background category.

Table 8-9

**Pre-Post SEA Counts and Rates of
Specific Delays in Development**

Variable: Specific Delays in Development
 Restrictions: Full Siblings of Ranch Hands and Comparisons
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted									
Time of Conception Relative to the Father's Duty in SEA									
Exposure Category	n	Pre-SEA Abn	Rate	n	Post-SEA Abn	Rate	Odds Ratio	Category Contract	p-Value
Background	1250	33	26.4	812	63	77.6	3.10	All Exp Categ	0.841
Unknown	514	15	29.2	221	18	81.4	2.95	Unk vs Bkgd	0.905
Low	244	8	32.8	148	17	114.9	3.83	Low vs Bkgd	0.670
High	148	6	40.5	195	16	82.1	2.12	High vs Bkgd	0.475

Hyperkinetic Syndrome of Childhood (All Children)

Model 1: Children of Ranch Hands - Log₂(Initial Dioxin)

Without adjustment for covariates (Table 8-10 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome and initial dioxin with time of conception among children of Ranch Hands with more than 10 ppt (p=0.172) or with more than 5 ppt (p=0.830) current dioxin.

Table 8-10

Pre-Post SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: All Children of Ranch Hands
Category: Time of Conception Relative to the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted								
		Time of Conception Relative to the Father's Duty in SEA						
Exposure Restriction	Initial Dioxin	n	Pre-SEA		n	Post-SEA		p-Value
			Abn	Rate		Abn	Rate	
a) D>10 ppt (n=1208)	Low	249	5	20.1	106	3	28.3	0.172
	Medium	338	6	17.8	245	7	28.6	
	High	113	0	0.0	157	6	38.2	
b) D>5 ppt (n=1748)	Low	286	2	7.0	155	10	64.5	0.830
	Medium	616	11	17.9	308	8	26.0	
	High	156	0	0.0	227	10	44.1	

Hyperkinetic Syndrome of Childhood (All Children)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$, and Time

Without adjustment for covariates (Table 8-11 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands having more than 10 ppt ($p=0.405$) or more than 5 ppt ($p=0.331$) current dioxin.

Table 8-11

Pre-Post SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: All Children of Ranch Hands
Category: Time of Conception Relative to the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Current Dioxin})$, Time

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n) Current Dioxin			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤18.6	21.9 (3/137)	21.9 (4/183)	0.0 (0/37)	0.405
		>18.6	10.5 (1/95)	17.5 (3/171)	0.0 (0/78)	
	Post-SEA	≤18.6	0.0 (0/62)	29.9 (4/134)	55.6 (4/72)	
		>18.6	50.0 (2/40)	37.0 (4/108)	21.5 (2/93)	
b) D>5 ppt	Pre-SEA	≤18.6	12.7 (2/157)	22.4 (7/313)	0.0 (0/66)	0.331
		>18.6	0.0 (0/150)	14.8 (4/270)	0.0 (0/102)	
	Post-SEA	≤18.6	33.3 (3/90)	28.7 (5/174)	54.5 (6/110)	
		>18.6	79.4 (5/63)	36.8 (5/136)	34.2 (4/117)	

Hyperkinetic Syndrome of Childhood (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-12), there is no significant variation in the overall association between hyperkinetic syndrome and categorized current dioxin with time of conception (p=0.161). The association between hyperkinetic syndrome and time of conception among children of Ranch Hands in the High current dioxin category is borderline significantly lower than that among children of Comparisons in the Background category (p=0.089) due to the lack of hyperkinetic pre-SEA children of fathers in the High dioxin category. The association between hyperkinetic syndrome and time of conception among children of Ranch Hands in the Low (p=0.238) and Unknown (p=0.614) categories are not significantly different from that among children of Comparisons in the Background category.

Table 8-12

Pre-Post SEA Counts and Rates of Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
 Restrictions: All Children of Ranch Hands and Comparisons
 Category: Time of Conception Relative to the Father's Duty in SEA
 Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted									
Time of Conception Relative to the Father's Duty in SEA									
Exposure Category	n	Pre-SEA		Post-SEA		Odds Ratio	Category Contract	p-Value	
		Abn	Rate	n	Abn	Rate			
Background	1459	19	13.0	981	32	32.6	2.56	All Exp Categ	0.161
Unknown	582	9	15.5	282	14	49.6	3.33	Unk vs Bkgd	0.614
Low	290	6	20.7	174	4	23.0	1.11	Low vs Bkgd	0.238
High	168	0	0.0	227	10	44.1	--	High vs Bkgd	0.089

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 1: Children of Ranch Hands - Log₂(Initial Dioxin)

Without adjustment for covariates (Table 8-13 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome and initial dioxin with time of conception among full sibling children of Ranch Hands with more than 10 ppt (p=0.245) or with more than 5 ppt (p=0.540) current dioxin.

Table 8-13

**Pre-Post SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood**

Variable: Hyperkinetic Syndrome of Childhood
 Restrictions: Full Siblings of Ranch Hands
 Category: Time of Conception Relative to the
 Father's Duty in SEA
 Model 1: Log₂(Initial Dioxin)

Ranch Hands - Log₂(Initial Dioxin) - Unadjusted									
Exposure Restriction	Initial Dioxin	n	Time of Conception Relative to the Father's Duty in SEA			n	Post-SEA		p-Value
			Pre-SEA Abn	Rate	Abn		Rate		
a) D>10 ppt (n=1030)	Low	231	5	21.6	78	2	25.6	0.245	
	Medium	276	5	18.1	206	5	24.3		
	High	103	0	0.0	136	4	29.4		
b) D>5 ppt (n=1489)	Low	252	2	7.9	114	10	87.7	0.540	
	Medium	545	10	18.3	245	5	20.4		
	High	135	0	0.0	198	7	35.4		

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 2: Children of Ranch Hands - Log₂(Current Dioxin), and Time

Without adjustment for covariates (Table 8-14 [a] and [b]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA and time of conception among full sibling children of Ranch Hands having more than 10 ppt (p=0.258) or more than 5 ppt (p=0.433) current dioxin.

Table 8-14

Pre-Post SEA Counts and Rates of Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
 Restrictions: Full Siblings of Ranch Hands
 Category: Time of Conception Relative to the Father's Duty in SEA
 Model 1: Log₂(Current Dioxin), Time

Ranch Hands - Log₂(Initial Dioxin) - Unadjusted						
Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n)			p-Value
			Low	Medium	High	
a) D>10 ppt	Pre-SEA	≤18.6	24.2 (3/124)	19.4 (3/155)	0.0 (0/35)	0.258
		>18.6	11.8 (1/85)	21.0 (3/143)	0.0 (0/69)	
	Post-SEA	≤18.6	0.0 (0/47)	17.4 (2/115)	31.3 (2/64)	
		>18.6	71.4 (2/28)	43.5 (4/92)	13.3 (1/75)	

Table 8-14 (Continued)

Exposure Restriction	Time of Conception	Time Since SEA (years)	Rate (No./n)			p-Value
			Low	Current Dioxin Medium	High	
b) D>5 ppt	Pre-SEA	≤18.6	15.9 (2/126)	21.7 (6/276)	0.0 (0/60)	0.433
		>18.6	0.0 (0/145)	16.9 (4/237)	0.0 (0/88)	
	Post-SEA	≤18.6	50.8 (3/59)	27.8 (4/144)	30.6 (3/98)	
		>18.6	94.3 (5/53)	37.7 (4/106)	30.9 (3/97)	

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-15), there is no significant variation in the overall association between hyperkinetic syndrome and categorized current dioxin with time of conception ($p=0.203$) in full siblings. Furthermore, the associations between hyperkinetic syndrome and time of conception among children of Ranch Hands in the High ($p=0.167$), Low ($p=0.256$) or Unknown ($p=0.358$) current dioxin categories are not significantly different from that among children of Comparisons in the Background category.

Table 8-15

Pre-Post SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: Full Siblings of Ranch Hands and Comparisons
Category: Time of Conception Relative to the
Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted									
Time of Conception Relative to the Father's Duty in SEA									
Exposure Category	n	Pre-SEA Abn	Pre-SEA Rate	n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contract	p-Value
Background	1250	19	15.2	812	29	35.7	2.40	All Exp Categ	0.203
Unknown	514	8	15.6	221	13	58.8	3.95	Unk vs Bkgd	0.358
Low	244	5	20.5	148	3	20.3	0.99	Low vs Bkgd	0.256
High	148	0	0.0	195	6	30.8	--	High vs Bkgd	0.167

8.3 Post-SEA Exposure Analyses

Analyses using Models 1, 2 and 3 were carried out in post-SEA children to determine if delays in development or hyperkinetic syndrome were associated with the father's dioxin body burden, with and without adjustment for covariates. The results, without and with restriction to full siblings, are summarized in tables 8-16 through 8-27.

Specific Delays in Development (All Children)

Model 1: Children of Ranch Hands - \log_2 (Initial Dioxin)

Without adjustment for covariates (Table 8-16 [a] and [b]), there is no significant association between specific delays in development and initial dioxin in children of Ranch Hands having more than 10 ppt ($p=0.321$) or more than 5 ppt ($p=0.758$) current dioxin.

After adjustment for covariates (Table 8-16 [c] and [d]), there is no significant association between specific delays in development and initial dioxin in children of Ranch Hands having more than 10 ppt current dioxin ($p=0.318$) or more than 5 ppt ($p=0.900$) current dioxin.

Table 8-16

Post-SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
Restrictions: All Children of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Initial Dioxin	n	Anomaly Number	Anomaly Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=508)	Low	106	12	113.2	0.88(0.67,1.14)	0.321
	Medium	245	25	102.0		
	High	157	10	63.7		
b) D>5 ppt (n=690)	Low	155	13	83.9	0.97(0.80,1.17)	0.758
	Medium	308	29	94.2		
	High	227	18	79.3		
Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Adjusted						
Exposure Restriction	Adj. Relative Risk (95% C.I.)		p-Value		Covariate Remarks	
c) D>10 ppt (n=458)	0.88(0.68,1.14)		0.318		C-TIME(p=0.061)	
d) D>5 ppt (n=616)	0.99(0.82,1.20)		0.900		C-TIME(p=0.005)	

Specific Delays in Development (All Children)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-17 [a]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.937$). Furthermore, there is no significant association between specific delays in development and current dioxin in children whose fathers had late ($p=0.429$) or early ($p=0.431$) tours.

Without adjustment for covariates (Table 8-17 [b]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA in children of Ranch Hands having more than 5 ppt current dioxin ($p=0.538$). Furthermore, there is no significant association between specific delays in development and current dioxin in children whose fathers had early ($p=0.624$) or late ($p=0.706$) tours.

After adjustment for covariates (Table 8-17 [c]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.812$). Furthermore, there is no significant association between specific delays in development and current dioxin in children whose fathers had late ($p=0.581$) or early ($p=0.376$) tours.

After adjustment for covariates (Table 8-17 [d]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.468$). Furthermore, there is no significant association between specific delays in development and current dioxin in children whose fathers had late ($p=0.616$) or early ($p=0.601$) tours.

Table 8-17

Post-SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
Restrictions: All Children of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 2: $\text{Log}_2(\text{Current Dioxin}), \text{Time}$

Ranch Hands - $\text{Log}_2(\text{Current Dioxin}), \text{Time}$ - Unadjusted						
Exposure Restriction	Time Since SEA (years)	Current Dioxin Anomaly Rate (No./n)			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
a) D>10 ppt (n=509)						0.937
	≤18.6	96.8 (6/62)	104.5 (14/134)	55.6 (4/72)	0.84(0.56,1.28)	0.429
	>18.6	100.0 (4/40)	111.1 (12/108)	75.3 (7/93)	0.86(0.60,1.24)	0.431
b) D>5 ppt (n=690)						0.538
	≤18.6	88.9 (8/90)	103.4 (18/174)	72.7 (8/110)	0.93(0.70,1.23)	0.624
	>18.6	47.6 (3/63)	110.3 (15/136)	68.4 (8/117)	1.05(0.80,1.38)	0.706

Table 8-17 (Continued)

Ranch Hands - Log₂(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=459)			0.812	C-TIME(p=0.059)
	≤18.6	0.78(0.31,1.92)	0.581	
	>18.6	0.83(0.55,1.25)	0.376	
d) D>5 ppt (n=616)			0.468	C-TIME(p=0.005)
	≤18.6	0.93(0.70,1.23)	0.616	
	>18.6	1.08(0.82,1.41)	0.601	

Specific Delays in Development (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-18 [a]), there is no significant overall association between specific delays in development and categorized current dioxin (p=0.293). However, the rate of specific delays in development among children of Ranch Hands in the Low category, 114.9 per 1000, is borderline significantly greater than the rate among children of Comparisons in the Background category, 72.4 per 1000 (p=0.057). The rates of specific delays in development among children of Ranch Hands in the High category (p=0.921) and among children of Ranch Hands in the Unknown category (p=0.475) are not significantly different from the rate in children of Comparisons in the Background category.

After adjustment for covariates (Table 8-18 [b]), there is no significant overall association between specific delays in development and categorized current dioxin (p=0.142). However, the rate of specific delays in development among children of Ranch Hands in the Low category, is significantly greater than the rate among children of Comparisons in the Background category (p=0.042). There is no significant difference between the rates of specific delays in development among children of Ranch Hands in the High category (p=0.682) or among children of Ranch Hands in the Unknown category (p=0.226) with the rate in children of Comparisons in the Background category.

Table 8-18

Post-SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
Restrictions: All Children of Ranch Hands and Comparisons
Children Conceived during or after the
Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted						
Exposure Category	n	Anomaly Number	Anomaly Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	981	71	72.4	All Exp Categ		0.293
Unknown	282	24	85.1	Unk vs Bkgd	1.19(0.74,1.93)	0.475
Low	174	20	114.9	Low vs Bkgd	1.66(0.98,2.81)	0.057
High	227	16	70.5	High vs Bkgd	0.97(0.55,1.71)	0.921
Total	1664					
b) Adjusted						
Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks	
Background	843	All Exp Categ		0.142	RACE(p=0.017)	
Unknown	246	Unk vs Bkgd	1.37(0.82,2.28)	0.226	OCC(p=0.005)	
Low	156	Low vs Bkgd	1.76(1.02,3.04)	0.042	SMOKE(p=0.031)	
High	203	High vs Bkgd	0.88(0.49,1.59)	0.682	C-TIME(p=0.004)	
Total	1448					

Specific Delays in Development (Full Siblings)

Model 1: Children of Ranch Hands - Log₂(Initial Dioxin)

Without adjustment for covariates (Table 8-19 [a] and [b]), there is no significant association between specific delays in development and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt (p=0.468) or more than 5 ppt (p=0.919) current dioxin.

After adjustment for covariates (Table 8-19 [c]), there is no significant association between specific delays in development and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt current dioxin (p=0.190) or with more than 5 ppt current dioxin (p=0.982).

Table 8-19

Post-SEA Counts and Rates of Specific Delays in Development

Variable: Specific Delays in Development
 Restrictions: Full Siblings of Ranch Hands
 Children Conceived during or after the Father's Duty in SEA
 Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Initial Dioxin	n	Anomaly Count	Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=420)	Low	78	10	128.2	0.90(0.68,1.19)	0.468
	Medium	206	21	101.9		
	High	136	10	73.5		
b) D>5 ppt (n=557)	Low	114	10	87.7	0.99(0.81,1.21)	0.919
	Medium	245	23	93.9		
	High	198	18	90.9		

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Adjusted			
Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=390)	0.82(0.60,1.11)	0.190	C-TIME(p=0.003) F-AGE(p=0.018) OCC(p=0.039)
d) D>5 ppt (n=513)	1.00(0.82,1.23)	0.982	C-TIME(p=(0.015)

Specific Delays in Development (Full Siblings)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-20 [a]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 10 ppt current dioxin ($p=0.704$). Furthermore, there is no significant association between specific delays in development and current dioxin in children of fathers who had late ($p=0.471$) or early ($p=0.815$) tours.

Without adjustment for covariates (Table 8-20 [b]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 5 ppt current dioxin ($p=0.530$). Furthermore, there is no significant association between specific delays in development and current dioxin in children of fathers who had late ($p=0.759$) or early ($p=0.557$) tours.

After adjustment for covariates (Table 8-20 [c]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 10 ppt current dioxin ($p=0.857$). Furthermore, there is no significant association between specific delays in development and current dioxin in children of fathers who had late ($p=0.541$) or early ($p=0.285$) tours.

After adjustment for covariates (Table 8-20 [d]), there is no significant variation in the association between specific delays in development and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 5 ppt current dioxin ($p=0.522$). Furthermore, there is no significant association between specific delays in development and current dioxin in children of fathers who had late ($p=0.591$) or early ($p=0.761$) tours.

Table 8-20

Post-SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 2: $\text{Log}_2(\text{Current Dioxin}), \text{Time}$

Ranch Hands - $\text{Log}_2(\text{Current Dioxin}), \text{Time}$ - Unadjusted						
Exposure Restriction	Time Since SEA (years)	Current Dioxin Anomaly Rate (No./n)			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
a) D>10 ppt (n=421)						0.704
	≤18.6	106.4 (5/47)	113.0 (13/115)	62.5 (4/64)	0.85(0.55,1.32)	0.471
	>18.6	107.1 (3/28)	97.8 (9/92)	93.3 (7/75)	0.95(0.65,1.41)	0.815
b) D>5 ppt (n=557)						0.530
	≤18.6	84.7 (5/59)	111.1 (16/144)	81.6 (8/98)	0.95(0.70,1.29)	0.759
	>18.6	56.6 (3/53)	103.8 (11/106)	82.5 (8/97)	1.09(0.82,1.46)	0.557

Table 8-20 (Continued)

Ranch Hands - Log₂(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=391)			0.857	C-TIME(p=0.003) OCC(p=0.032) F-AGE(p=0.026)
	≤18.6	0.73(0.26,2.01)	0.541	
	>18.6	0.77(0.48,1.24)	0.285	
d) D>5 ppt (n=513)			0.522	C-TIME(p=0.014)
	≤18.6	0.83(0.42,1.64)	0.591	
	>18.6	0.95(0.70,1.29)	0.761	

Specific Delays in Development (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-21 [a]), there is no significant overall association between specific delays in development and categorized current dioxin among full siblings (p=0.550). Furthermore, there is no significant difference between the rate of specific delays in development in children of Ranch Hands in the High (p=0.835), Low (p=0.134) or Unknown (p=0.850) categories and the rate in children of Comparisons in the Background category.

After adjustment for covariates (Table 8-21 [b]), there is no significant variation in the overall association between specific delays in development and categorized current dioxin with the father's age at the time of conception (p=0.006) and the time of conception (p=0.005). The basis for this variation is displayed in Appendix Table F-1. There is a significantly elevated risk in children of Ranch Hands in the Low category (OR=6.48, 95% CI 1.78-23.5, p=0.004) conceived within 4 years of duty in SEA whose father was more than 30 years old at the time of conception. In the same stratum, the contrast of children of Ranch Hands in the High category with children of Comparisons in the Background category was of borderline significance (p=0.099), as was the contrast of children of Ranch Hands in the Unknown category with children of Comparisons in the Background category (p=0.075). The contrasts with the Background category are not significant in the remaining strata.

Table 8-21

Post-SEA Counts and Rates of
Specific Delays in Development

Variable: Specific Delays in Development
Restrictions: Full Siblings of Ranch Hands and Comparisons
Children Conceived during or after the
Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted						
Exposure Category	n	Anomaly Count	Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	812	63	77.6	All Exp Categ		0.550
Unknown	221	18	81.4	Unk vs Bkgd	1.05(0.61,1.82)	0.850
Low	148	17	114.9	Low vs Bkgd	1.54(0.88,2.72)	0.134
High	195	16	82.1	High vs Bkgd	1.06(0.60,1.88)	0.835
Total	1376					
b) Adjusted						
Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate	Remarks
Background	715	All Exp Categ		****	RACE	(p=0.004)
Unknown	199	Unk vs Bkgd	****	****	SMOKE	(p=0.002)
Low	137	Low vs Bkgd	****	****	DIOXIN*F-AGE	(p=0.006)
High	180	High vs Bkgd	****	****	DIOXIN*C-TIME	(p=0.005)
Total	1231					

Hyperkinetic Syndrome of Childhood (All Children)

Model 1: Children of Ranch Hands - Log₂(Initial Dioxin)

Without adjustment for covariates (Table 8-22 [a] and [b]), there is no significant association between hyperkinetic syndrome and initial dioxin among children of Ranch Hands having more than 10 ppt (p=0.939) or more than 5 ppt (p=0.277) current dioxin.

After adjustment for covariates (Table 8-22 [c] and [d]), there is no significant association between hyperkinetic syndrome and initial dioxin among children of Ranch Hands having more than 10 ppt (p=0.988) or more than 5 ppt (p=0.162) current dioxin.

Table 8-22

Post-SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: All Children of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Initial Dioxin	n	Anomaly Count	Anomaly Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=508)	Low	106	3	28.3	1.02(0.67,1.55)	0.939
	Medium	245	7	28.6		
	High	157	6	38.2		
b) D>5 ppt (n=690)	Low	155	10	64.5	0.86(0.65,1.14)	0.277
	Medium	308	8	26.0		
	High	227	10	44.1		
Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Adjusted						
Exposure Restriction	Adj. Relative Risk (95% C.I.)		p-Value		Covariate Remarks	
c) D>10 ppt (n=458)	0.99(0.64,1.55)		0.988		RACE(p=0.094)	
d) D>5 ppt (n=616)	0.81(0.60,1.10)		0.162		RACE(p=0.030)	

Hyperkinetic Syndrome of Childhood (All Children)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-23 [a]), there is borderline significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA among children of Ranch Hands with more than 10 ppt current dioxin ($p=0.086$). There is no significant association between hyperkinetic syndrome and dioxin in children of Ranch Hands who had late tours ($p=0.142$) and no significant risk among children of Ranch Hands who had early tours ($p=0.359$). The borderline significant interaction is caused by an increasing trend in children of fathers with late tours and a decreasing trend in children of fathers with early tours, but neither of these trends are significant.

Without adjustment for covariates (Table 8-23 [b]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.139$). There is no significant association between hyperkinetic syndrome and current dioxin in children of fathers who had late ($p=0.679$) tours. However, there is a borderline significant association between hyperkinetic syndrome and current dioxin in children of fathers who had early ($p=0.101$) tours; in that stratum, the rate of hyperkinetic syndrome decreases with dioxin.

After adjustment for covariates (Table 8-23 [c]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin ($p=0.191$). Furthermore, there is no significant association between hyperkinetic syndrome and current dioxin in children of fathers who had late ($p=0.320$) or early ($p=0.402$) tours.

After adjustment for covariates (Table 8-23 [d]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA among children of Ranch Hands having more than 5 ppt current dioxin ($p=0.490$). Furthermore, there is no significant association between hyperkinetic syndrome and current dioxin in children of fathers who had late ($p=0.683$) or early ($p=0.154$) tours.

Table 8-23

**Post-SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood**

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: All Children of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 2: $\text{Log}_2(\text{Current Dioxin}), \text{Time}$

Ranch Hands - $\text{Log}_2(\text{Current Dioxin}), \text{Time}$ - Unadjusted						
Exposure Restriction	Time Since SEA (years)	Current Dioxin Anomaly Rate (No./n)			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
a) D>10 ppt (n=509)						0.086
	≤18.6	0.0 (0/62)	29.9 (4/134)	55.6 (4/72)	1.61(0.85,3.04)	0.142
	>18.6	50.0 (2/40)	37.0 (4/108)	21.5 (2/93)	0.74(0.40,1.40)	0.359
b) D>5 ppt (n=690)						0.139
	≤18.6	33.3 (3/90)	28.7 (5/174)	54.5 (6/110)	1.09(0.72,1.64)	0.679
	>18.6	79.4 (5/63)	36.8 (5/136)	34.2 (4/117)	0.70(0.46,1.07)	0.101

Table 8-23 (Continued)

Ranch Hands - Log₂(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=459)			0.191	None
	≤18.6	1.44(0.70,2.96)	0.320	
	>18.6	0.77(0.42,1.42)	0.402	
d) D>5 ppt (n=616)			0.490	RACE(p=0.037)
	≤18.6	0.91(0.58,1.42)	0.683	
	>18.6	0.74(0.48,1.12)	0.154	

Hyperkinetic Syndrome of Childhood (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-24 [a]), there is no significant overall association between hyperkinetic syndrome and categorized current dioxin (p=0.383). Furthermore, there is no significant difference between the rate of hyperkinetic syndrome in children of Ranch Hands in the High (p=0.399), Low (p=0.503) or Unknown (p=0.180) categories with the rate in children of Comparisons in the Background category.

After adjustment for covariates (Table 8-24) [b], there is no significant overall association between hyperkinetic syndrome and categorized current dioxin (p=0.618). Furthermore, there is no significant difference between the rates of hyperkinetic syndrome in children of Ranch Hands in the High (p=0.902), Low (p=0.539) or Unknown (p=0.289) categories and the rate in children of Comparisons in the Background category.

Table 8-24

Post-SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: All Children of Ranch Hands and Comparisons
Children Conceived during or after the
Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Anomaly Count	Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	981	32	32.6	All Exp Categ		0.383
Unknown	282	14	49.6	Unk vs Bkgd	1.55(0.81,2.95)	0.180
Low	174	4	23.0	Low vs Bkgd	0.70(0.24,2.00)	0.503
High	227	10	44.1	High vs Bkgd	1.37(0.66,2.82)	0.399
Total	1664					

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	843	All Exp Categ		0.618	RACE(p=0.095)
Unknown	246	Unk vs Bkgd	1.43(0.74,2.79)	0.289	DRINK(p=0.045)
Low	156	Low vs Bkgd	0.72(0.25,2.07)	0.539	C-TIME(p=0.047)
High	203	High vs Bkgd	1.05(0.47,2.33)	0.902	
Total	1448				

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 1: Children of Ranch Hands - Log₂(Initial Dioxin)

Without adjustment for covariates (Table 8-25 [a] and [b]), there is no significant association between hyperkinetic syndrome and initial dioxin among full sibling children of Ranch Hands having more than 10 ppt (p=0.892) and a borderline significant negative association between hyperkinetic syndrome and initial dioxin among full sibling children of Ranch Hands having more than 5 ppt (p=0.058) current dioxin.

After adjustment for covariates (Table 8-25 [c] and [d]), there is no significant association between hyperkinetic syndrome and initial dioxin among full sibling children of Ranch Hands having more than 10 ppt (p=0.880); however, there is a significant negative association between hyperkinetic syndrome and initial dioxin among full sibling children of Ranch Hands having more than 5 ppt (p=0.053).

Table 8-25

Post-SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 1: $\text{Log}_2(\text{Initial Dioxin})$

Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Unadjusted						
Exposure Restriction	Initial Dioxin	n	Anomaly Count	Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=420)	Low	78	2	25.6	0.96(0.58,1.61)	0.892
	Medium	206	5	24.3		
	High	136	4	29.4		
b) D>5 ppt (n=557)	Low	114	10	87.7	0.73(0.52,1.03)	0.058
	Medium	245	5	20.4		
	High	198	7	35.4		
Ranch Hands - $\text{Log}_2(\text{Initial Dioxin})$ - Adjusted						
Exposure Restriction	Adj. Relative Risk (95% C.I.)		p-Value		Covariate Remarks	
c) D>10 ppt (n=390)	0.96(0.58,1.60)		0.880		None	
d) D>5 ppt (n=513)	0.73(0.52,1.02)		0.053		None	

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 2: Children of Ranch Hands - $\text{Log}_2(\text{Current Dioxin})$ and Time

Without adjustment for covariates (Table 8-26 [a]), there is borderline significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 10 ppt current dioxin ($p=0.102$). However, there is no significant association between hyperkinetic syndrome and current dioxin in children of fathers who had late ($p=0.267$) or early ($p=0.231$) tours. The borderline significant interaction was caused by an increasing trend in children of fathers with late tours and a decreasing trend in children of fathers with early tours, but neither of these trends were significant.

Without adjustment for covariates (Table 8-26 [b]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA of duty among full sibling children of Ranch Hands having more than 5 ppt current dioxin ($p=0.594$). There is no significant association between hyperkinetic syndrome and current dioxin in children of Ranch Hands who had late ($p=0.410$) tours; however, there is a borderline significant negative association between hyperkinetic syndrome and current dioxin in children of Ranch Hands who had early tours ($p=0.082$).

After adjustment for covariates (Table 8-26 [c]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 10 ppt current dioxin ($p=0.114$). Furthermore, there is no significant association between hyperkinetic syndrome and current dioxin in children of Ranch Hands who had late ($p=0.285$) or early ($p=0.245$) tours.

After adjustment for covariates (Table 8-26 [d]), there is no significant variation in the association between hyperkinetic syndrome and current dioxin with time since duty in SEA among full sibling children of Ranch Hands having more than 5 ppt current dioxin ($p=0.631$). There is no significant association between hyperkinetic syndrome and current dioxin in children of Ranch Hands who had late ($p=0.372$) tours, however, there is a borderline significant negative association between hyperkinetic syndrome and current dioxin in children of Ranch Hands who had early tours ($p=0.082$).

Table 8-26

Post-SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the
Father's Duty in SEA
Model 2: $\text{Log}_2(\text{Current Dioxin}), \text{Time}$

Ranch Hands - $\text{Log}_2(\text{Current Dioxin}), \text{Time}$ - Unadjusted						
Exposure Restriction	Time Since SEA (years)	Current Dioxin Anomaly Rate (No./n)			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
a) D>10 ppt (n=421)						0.102
	≤18.6	0.0 (0/47)	17.4 (2/115)	31.3 (2/64)	1.65(0.68,4.02)	0.267
	>18.6	71.4 (2/28)	43.5 (4/92)	13.3 (1/75)	0.64(0.31,1.33)	0.231
b) D>5 ppt (n=557)						0.594
	≤18.6	50.8 (3/59)	27.8 (4/144)	30.6 (3/98)	0.80(0.47,1.36)	0.410
	>18.6	94.3 (5/53)	37.7 (4/106)	30.9 (3/97)	0.66(0.42,1.05)	0.082

Table 8-26 (Continued)

Ranch Hands - Log₂(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=391)			0.114	None
	≤18.6	1.62(0.67,3.92)	0.285	
	>18.6	0.66(0.32,1.33)	0.245	
d) D>5 ppt (n=513)			0.631	None
	≤18.6	0.79(0.46,1.33)	0.372	
	>18.6	0.66(0.42,1.05)	0.082	

Hyperkinetic Syndrome of Childhood (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 8-27 [a]), there is no significant overall association between hyperkinetic syndrome and categorized current dioxin among full sibling children (p=0.244). Furthermore, there is no significant difference between the rate of hyperkinetic syndrome among children of Ranch Hands in the High (p=0.735), Low (p=0.342) or Unknown (p=0.126) categories and the rate in children of Comparisons in the Background category.

After adjustment for covariates (Table 8-27 [b]), there is no significant overall association between hyperkinetic syndrome and categorized current dioxin among full sibling children (p=0.220). Furthermore, there is no significant difference between the rates of hyperkinetic syndrome among children of Ranch Hands in the High (p=0.715), Low (p=0.330) or Unknown (p=0.119) categories and the rate in children of Comparisons in the Background category.

Table 8-27

Post-SEA Counts and Rates of
Hyperkinetic Syndrome of Childhood

Variable: Hyperkinetic Syndrome of Childhood
Restrictions: Full Siblings of Ranch Hands and Comparisons
Children Conceived during or after the
Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Anomaly Count	Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	812	29	35.7	All Exp Categ		0.244
Unknown	221	13	58.8	Unk vs Bkgd	1.69(0.86,3.31)	0.126
Low	148	3	20.3	Low vs Bkgd	0.56(0.17,1.86)	0.342
High	195	6	30.8	High vs Bkgd	0.86(0.35,2.10)	0.735
Total	1376					

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	715	All Exp Categ		0.220	DRINK(p=0.087)
Unknown	199	Unk vs Bkgd	1.71(0.87,3.38)	0.119	M-AGE(p=0.053)
Low	137	Low vs Bkgd	0.55(0.16,1.83)	0.330	C-TIME(p=0.051)
High	180	High vs Bkgd	0.85(0.34,2.08)	0.715	
Total	1231				

8.4 Conclusion

Throughout this section, nonsignificant results are indicated by NS, borderline significant results are indicated by NS* and the presence of interactions with the p-value greater than or equal to 0.01 and less than 0.05 are indicated with a preceding double asterisk (**). Four asterisks (****) represent the presence of an interaction between a covariate and dioxin with a p-value less than 0.01.

Twelve selected birth defects: anencephaly, spina bifida, hydrocephalus, cleft palate, cleft lip/palate, esophageal atresia, anorectal atresia, polydactyly, limb reduction deformities, hypospadias, congenital hip dislocation, Down's syndrome, and 4 developmental disabilities: disturbance of emotion specific to childhood and adolescence, hyperkinetic syndrome of childhood, specific delays in development and mental retardation were considered for investigation. Of these, there were only enough occurrences of specific delays in development and hyperkinetic syndrome to permit assessment of associations with dioxin. There were too few occurrences in the other categories to permit any statistical analysis.

Assessments of the association between specific delays in development and hyperkinetic syndrome and dioxin were carried out based on all children (pre-SEA and post-SEA) using Models 1, 2 and 3. Each analysis was carried out without adjustment for covariates. All analyses were first based on all children and again full siblings. The results are summarized in Tables 8-28 through 8-30.

Table 8-28

P-Value Summary of Initial Dioxin (Model 1) Pre-Post SEA Analyses
of Specific Delays in Development and Hyperkinetic Syndrome
of Childhood (Children of Ranch Hands)

a) All Children		
Anomaly	Unadjusted	
	D>10 ppt	D>5 ppt
Specific Delays in Development	0.035	0.044
Hyperkinetic Syndrome of Childhood	NS	NS
b) Full Siblings		
Anomaly	Unadjusted	
	D>10 ppt	D>5 ppt
Specific Delays in Development	0.045	0.053
Hyperkinetic Syndrome of Childhood	NS	NS

Table 8-29

P-Value Summary of Current Dioxin and Time Pre-Post SEA Analyses
(Model 2) of Specific Delays in Development and Hyperkinetic
Syndrome of Childhood (Children of Ranch Hands)

a) All Children		
Anomaly	Unadjusted	
	D>10 ppt	D>5 ppt
Specific Delays in Development	NS*	0.032
Hyperkinetic Syndrome of Childhood	NS	NS

b) Full Siblings		
Anomaly	Unadjusted	
	D>10 ppt	D>5 ppt
Specific Delays in Development	NS*	NS*
Hyperkinetic Syndrome of Childhood	NS	NS

Table 8-30

P-Value Summary of Pre-Post-SEA Categorized Current Dioxin (Model 3)
Analyses of Specific Delays in Development and Hyperkinetic
Syndrome of Childhood (Children of Ranch Hands and Comparisons)

a) All Children				
Anomaly	All	Unadjusted		
		Contrasts Unknown	with Background Low	High
Specific Delays in Development	NS	NS	NS	NS
Hyperkinetics Syndrome of Childhood	NS	NS	NS	NS*

b) Full Siblings				
Anomaly	All	Unadjusted		
		Contrasts Unknown	with Background Low	High
Specific Delays in Development	NS	NS	NS	NS
Hyperkinetics Syndrome of Childhood	NS	NS	NS	NS

Assessment of the association between specific delays in development and hyperkinetic syndrome and dioxin were also carried out based on post-SEA children using Models 1 2 and 3. Each analysis was carried out without and then with adjustment for covariates. All analyses were first based on all post-SEA children and again on only the post-SEA full sibling children. The results are summarized in Tables 8-31 through 8-33.

Table 8-31

P-Value Summary of Post-SEA Initial Dioxin Analyses (Model 1)
of Specific Delays in Development and Hyperkinetic
Syndrome of Childhood (Children of Ranch Hands)

a) All Children				
Anomaly	Unadjusted		Adjusted	
	D>10 ppt	D>5 ppt	D>10 ppt	D>5 ppt
Specific Delays in Development	NS	NS	NS	NS
Hyperkinetic Syndrome of Childhood	NS	NS	NS	NS
b) Full Siblings				
Anomaly	Unadjusted		Adjusted	
	D>10 ppt	D>5 ppt	D>10 ppt	D>5 ppt
Specific Delays in Development	NS	NS	NS	NS
Hyperkinetic Syndrome of Childhood	NS	NS*	NS	0.053

Table 8-32

P-Value Summary of Post-SEA Current Dioxin and Time Analyses (Model 2)
of Specific Delays in Development and Hyperkinetic
Syndrome of Childhood (Children of Ranch Hands)

a) All Children

Anomaly	Unadjusted					
	Dioxin by Time	D>10 ppt Time Since SEA (years)		Dioxin by Time	D>5 ppt Time Since SEA (years)	
		≤18.6	>18.6		≤18.6	>18.6
Specific Delays in Development	NS	NS	NS	NS	NS	NS
Hyperkinetic Syndrome of Childhood	NS*	NS	NS	NS	NS	NS*

b) Full Siblings

Anomaly	Unadjusted					
	Dioxin by Time	D>10 ppt Time Since SEA (years)		Dioxin by Time	D>5 ppt Time Since SEA (years)	
		≤18.6	>18.6		≤18.6	>18.6
Specific Delays in Development	NS	NS	NS	NS	NS	NS
Hyperkinetic Syndrome of Childhood	NS*	NS	NS	NS	NS	NS*

c) All Children

Anomaly	Adjusted					
	Dioxin by Time	D>10 ppt Time Since SEA (years)		Dioxin by Time	D>5 ppt Time Since SEA (years)	
		≤18.6	>18.6		≤18.6	>18.6
Specific Delays in Development	NS	NS	NS	NS	NS	NS
Hyperkinetic Syndrome of Childhood	NS	NS	NS	NS	NS	NS

Table 8-32 (Continued)

d) Full Siblings

Anomaly	Adjusted					
	Dioxin by Time	D>10 ppt Time Since SEA (years)		Dioxin by Time	D>5 ppt Time Since SEA (years)	
		≤18.6	>18.6		≤18.6	>18.6
Specific Delays in Development	NS	NS	NS	NS	NS	NS
Hyperkinetic Syndrome of Childhood	NS	NS	NS	NS	NS	NS*

Table 8-33

P-Value Summary of Post-SEA Categorized Current Dioxin Analyses
(Model 3) of Specific Delays in Development and Hyperkinetic Syndrome
of Childhood (Children of Ranch Hands and Comparisons)

a) All Children

Anomaly	All	Unadjusted		
		Contrasts with Background		
		Unknown	Low	High
Specific Delays in Development	NS	NS	NS*	NS
Hyperkinetic Syndrome of Childhood	NS	NS	NS	NS

b) All Children

Anomaly	All	Adjusted		
		Contrasts with Background		
		Unknown	Low	High
Specific Delays in Development	NS	NS	0.042	NS
Hyperkinetic Syndrome of Childhood	NS	NS	NS	NS

Table 8-33 (Continued)

c) Full Siblings

Anomaly	Unadjusted			
	All	Unknown	Contrasts with Background Low	High
Specific Delays in Development	NS	NS	NS	NS
Hyperkinetic Syndrome of Childhood	NS	NS	NS	NS

d) Full Siblings

Anomaly	Adjusted			
	All	Unknown	Contrasts with Background Low	High
Specific Delays in Development	****	****	****	****
Hyperkinetic Syndrome of Childhood	NS	NS	NS	NS

Pre-post SEA analyses of hyperkinetic syndrome of childhood were entirely negative. Unadjusted Model 1 and 2 analyses of specific delays in development found significant associations but these were not supportive of a hypotheses that dioxin is adversely associated with delays in development; the corresponding adjusted analyses were negative. The Model 1 findings were caused by a reversal of pre-SEA and post-SEA trends with dioxin; the pre-SEA rates were increasing and the post-SEA rates decreased or did not increase with dioxin. The Model 2 finding was caused by high post-SEA rates of delays in development in children of Ranch Hands with intermediate dioxin levels and low rates in children of Ranch Hands with high dioxin levels. These patterns are not consistent with the expected dose-response, are inconsistent with each other and are most likely chance occurrences.

Analyses of post-SEA hyperkinetic syndrome of childhood found one significant association in an adjusted Model 1 analysis restricted to full sibling children. This finding was caused by a decreasing rate of hyperkinetic syndrome with dioxin in children of Ranch Hands having more than 5 ppt current dioxin. This finding is opposite to the expected dose-response and is most likely due to chance.

Analyses of post-SEA specific delays in development found one significant association in an adjusted Model 3 analysis. This finding was caused by the rate of delays in development being higher in children of Ranch Hands in the Low dioxin category than in children of Comparisons in the Background category. The rate in children of Ranch Hands in the High dioxin category was not significantly different from the rate in children of Comparisons in the Background category.

A significant interaction with the father's age at the time of birth of the child and the time of conception relative to the father's SEA duty was found in a Model 3 analysis of specific delays in development. This interaction was caused by a significantly high rate in children of Ranch Hands in the Low dioxin category 30 years of age or younger and with the time of conception within 4 years of the father's departure from SEA as compared with the rate in corresponding children of Comparisons in the Background category. Analyses within the other 3 strata determined by the father's age and the time of conception were negative.

These findings are weak, inconsistent and sometimes opposite to the expected dose response. They are therefore not supportive of a hypothesis of an adverse association between dioxin and delays in development or hyperkinetic syndrome. There was insufficient data to assess the association between dioxin and the other 12 anomalies and 2 developmental disorders considered in this chapter.