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Evaluation of Veterans for Agent Orange Exposure

M. R. Flicker and A. L. Young

Veterans Administration	Agent Orange Projects Office
Medical Center	Veterans Administration
4801 Linwood Boulevard	810 Vermont Avenue, N.W.
Kansas City, MO 64128	Washington, D.C. 20420

The Veterans Administration has been evaluating Vietnam veterans for signs and symptoms of adverse health effects attributable to phenoxyherbicide and dioxin exposure.

Agent Orange Registry: Preliminary data collection began as the Agent Orange Registry in 1978. Any veteran concerned about health effects of Agent Orange could report to a VA hospital for a complete medical and exposure history, physical examination and selected laboratory tests. The names, addresses and results of the evaluations were compiled by computer in the hopes of identifying any trends in symptomatology or health.

Rationale for the Registry Exam: The importance of the complete history taking from involved veterans becomes apparent upon a review of the known toxicology of the herbicides and TCDD. Veterans were being evaluated from ten to twenty years after alleged exposure; adverse health effects of 2,4-D and 2,4,5-T should manifest themselves shortly after exposure and -- as in the case of the peripheral neuropathies -- persist at most up to three years. In addition, toxic effects of TCDD are rarely present in the absence of chloracne, which itself only rarely persist up to ten to twenty years. Thus, the majority of veterans -- even if heavily exposed -- would be expected to have no or few residual signs or symptoms at the time of their Agent Orange evaluation.

A complete history is also essential to avoid confusing the effects of other toxins such as alcohol with those of Agent Orange, for the human body has only a finite number of responses to a large number of toxic agents.

Special Features of the Agent Orange Exam: In addition to the standard medical history, veterans were asked about their recollections of known herbicide and toxic chemical exposure, frequency, intensity and duration as well as any history of neoplasic infertility, abortion or teratogenesis in themselves or their families.

Laboratory testing included hematologic, hepatic and radiographic analysis. When necessary, nerve conduction studies and sperm counts were obtained.

Summary of Known Health Effects of 2,4-D and 2,4,5-T and TCDD: In order to assess the forthcoming data from the Agent Orange registry, the following summary is relevant:

1. 2,4-D -- peripheral neuropathy (most important), neuropenia and acute gastrointestinal effects (nausea, vomitting) and headache;

2. 2,4,5-T and TODD — chloracne, a form of acne often clinically indistinguishable from acne vulgaris; porphyria cutanea tarda: hyperpigmentation, hirsutism, hepatic dysfunction; asthenia: a symptom complex closely associated with depression and difficult to distinguish from the post traumatic stress disorder seen after all wars and catastrophes (headache, apathy, fatigue, sleep disturbance, anorexia and decreased learning ability). Normally expected to clear with time.

Symptoms arising for the first time months and years post exposure are probably due to an etiology other than 2,4-D and 2,4,5-T. The question of carcinogenesis, teratogenesis and mutageneis remains open; to date there is no proven association in humans.

Summary of Registry Results: Although the registry participants comprise a self-selected group, the composition of the registrants by service branch accurately reflects the relative population of that branch in Vietnam:

Army	668
Marine Corps	20%
Air Force	78
Navy	68
Other	1୫

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To date, over 110,000 veterans have been evaluated. Approximately three quarters of them complained of symptoms of illness. These symptoms and their relative frequency are characterized below:

Symptom Category	Percent of Registered Patients
Dermatologic	40
Psychologic	25
Headache	13
Peripheral Neuropathy	12
Asthenia	12
Gastrointestinal	12
Sexual Dysfunction	5
Other	44

Of the several thousand veterans complaining of dermatologic problems, only one may possibly turn out to be chloracne.

Many of the psychiatric/asthenic patients have been variants of the delayed stress response syndrome seen after all major wars.

Noteworthy is that the majority of the above symptoms bear no correlation to the known toxicology of Herbicide Orange; in addition, no increased incidence of malignancy have been observed in this population which, by virtue of its self-selected nature, may have been expected to exhibit artificially higher than baseline rates in the general population.

Supporting the above data is the observation by the Armed Forces Institutes of Pathology that there is no unusual clustering or incidence of tumor among the over twelve hundred pathological specimens from Vietnam veterans examined to date.

Conclusions: Thus, the Agent Orange Registry data do not support the thesis that there is any unusual long-term morbidity associated with Vietnam service or Agent Orange exposure.

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DISTRIBUTION OF AGENT ORANGE EXAMINATIONS BY YEAR

Year of Exam	Number	Percentage
1978	463	0.6
1979	5033	5.9
1980	27574	32.6
1981	25592	30.3
1982	22410	26.5
1983	3195	3.8
unknown	169	0.2
Total	84456	100

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COMPARISON OF DISTRIBUTION OF EXAMINEES BY BRANCH OF SERVICE WITH DISTRIBUTION IN DEPARTMENT OF DEFENSE DATA

D., 1., 6		Percent	age In
Branch of Service	Number	AO Registry	DoD Data
Anny	56594	67.0	67.2
Marines	15373	18.2	13.6
Air Force	6514	7.7	12.7
Navy	5101	6.0	6.3
Coast Guard	76	.1	. 1
Other/Not. Specified	798	0.9	-
Total	84456	100	100

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DISTRIBUTION OF EXAMINERS BY SELF REPORTED EXPOSURES

Number of Exposures	Number	Percentage
More than 2	22916	27.1
1 or 2	6344	7.5
Not Specified	47455	56.2
Other	7741	9.2
Total	84456	100.0

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DISTRIBUTION OF TYPE OF EXPOSURE REPORTED BY EXAMINEES

Type of Exposure	Number	Percentage
During Actual Spraying	9453	11.2%
While handling Agent Orange	2734	3.2
While passing through defoliated area	49722	58.9
Unsure of actual exposure	9109	10.8
Other	2855	3.4
Unspecified	10585	12.5
	<u> </u>	<u></u>

Total

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84456

100.0

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DISTRIBUTION OF EXAMINERS BY LENGTH OF EXPOSURE

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Exposure	Nunber	Percentage	
Under 2 month	8786	10-4	
2-6 months	7453	8.8	
Over 6 months	29135	34.5	
Not Specified/Unknown	39082	46.5	

Complaint	Nuaber	Percentage
Skin Rash	32846	38.9
Nervousness	44825	17.6
Headaches	11874	14.1
Abdominal Complaints	10239	12.1
Personality Disorders	8614	10.2
	-	

FIVE MOST FREQUENT COMPLAINTS

NUMBER AND PERCENTAGE OF VETERANS REPORTING REPRODUCTIVE PROBLEMS

Reproductive Problems	Number	Percentage
Infertility	4106	4.9
Abortions	11293	13.4
Teratogenesis	4477	5.3
Birth Defects/Child Death	5313	6.3

MOST FREQUENT FINDINGS REPORTED

Finding	Number	Reccentage
No abnormalities	24563	29.18
Abnormalities:		
Skin	31675	37.5
Extremities	9151	10.8
Nose, throat oral cavity	7242	8 .6
Mental status	7183	8.5

MOST FREQUENT DIAGNOSES

Diagnosis	Nunber	Percentage
No Diagnosis	35957	42.68
Skin Disease	22147	26.2
Mental Disorders	8783	10.4
Dis. of the Musculo-Skeletal System	5778	6.8
Dis. of the Sensory Organs	3520	4.2

		(PDIS-DATE	NSCHO J		Б	
Complaint	Army	Marines	Air Force	Navy	Coast Guard	Unknown Other
Skin rash	39.1	39.5	33. 23.1	36.3	38.2	36.6
Nervousness	17.9	18.7	14.2	14.5	· 17 . 1	17.6
Beadaches	14.1 ·	15.1	12.6	12.3	15.8	12.7
Abdominal complaints	12.0	13.3	11.6	10.8	21.0	8-4
Personality problems	9.9	12.1	8-8	8.9	14.5	7.5
Numbriess	8.2	8.9	8.0	8.3	10.5	7.5
Muscle aching, tingling	8.1	8.1	8.7	8.0	15_8	5.1
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MOST FREQUENT COMPLAINTS BY BRANCH OF SERVICE (PERCENTAGES)

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MOST FREQUENT ABNORMAL FINDINGS BY BRANCH OR SERVICE (PERCENTAGES)

Findings	Anny	Marines	Air Force	Navy	Coast Guard	Other
No Abnormalities	29.0	29.1	29.1	30.2	23.7	27.5
Abnormality of:						
Skin	37.9	37.8	35.8	35.8	38.2	28.9
Extremities	10.5	12.2	10.8	10.5	10.5	7.9
Mental Condition Nose, throat, and	8.6	9.6	6.5	7.0	13.2	5.2
oral cavity	8.7	8.4	8.7	8.5	11.8	5.0
Abdomen	6.7	6.7	6.9	6.2	17.1	5.2

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MOST FREQUENT DIAGNOSES BY BRANCH OF SERVICE (PERCENTAGES)

Diagnosis	Аслу	Marines	Air Force	Navy	Coast Guard	Other/ Unknown
1 :						
No diagnoses	42.5	42.9	41.9	43.2	35.5	46.7
Dis. of skin/sub-	•					
contaneous tissue	26.2	26.5	26.3	25.3	23.7	21.7
Mental disorder	10.6	11.7	7.8	8.3	13.2	7.5
Dis. of bones, joints, tendons	6.7	6.7	8.2	6.7	3.9	6.5
Dis of senory organs	4.2	4.3	4.1	3 .9	2.6	2.8
Alcoholism	3.4	3.5	2.7	3.1	3.9	2.5
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COMPLAINTS BY EXPOSURE GROUPS (PERCENTAGES)

	Exposure Group		
Complaint	High	Low	Other
Nervousness	25.3	16.0	16.2
Weakness	7.8	3.0	3.8
Fatigue	10.4	5.0	5.1
Muscle Aches	12.9	6.3	7.3
Numbress	12.8	7.0	7.5
Sexual Dysfunction	7.1	4.3	3.9
Personality Problems	16.1	7.8	9.2
Abdominal Complaints	17.8	11.0	11.1
Dental Complaints	6.2	2.7	3.1
Fever	5.2	2.0	2.7
Skin Rash	48.6	35.2	37.2
Beadache	19-2	12.7	13.2
Hair Loss	3.8	2.2	2.2
Other	42.8	32.2	36.4
	······		al
Number of Cases	12821	2576	69059

SELF REPORTED REPRODUCTIVE PROBLEMS BY EXPOSURE GROUP

	Exp	osure Group		
Problems	fligh	Low	Other	-,
Reported Evidence of:				
Infertility	5.9	4.9	4.8	
Abortions	14.5	13.4	13.4	
Teratogenesis	6.3	5.3	5.2	
Birth Defects/Infant Death	7.1	6.2	6.3	

ABNORMAL FINDINGS BY EXPOSURE GROUP (PERCENTAGE)

Exposure Group

Abnormality	High	Low	Other
Vital Signs	4.5	3.8	3.6
General Apperance	5.1	4.5	5.2
Mental Status	11.8	8.1	7.9
Head/Neck	4.3	3.8	3.4
Eyes	5.4	5.3	5.0
Ears	7.3	6.2	5.5
Nose, Throat, Mouth	10.1	8.7	8.3
Lungs	3.7	2.8	3.0
Heart.	3.5	2.5	
Abdomen	9.1	6.5	6.3
Hernia Genitala	1.6 4.4 4.0	1.0	1.3
		4.0	4.0
Rectum		3.8	3.7
Prostate	1.7	1.4	1.4
Back	5.8	4.3	4.1
Extremities	13.0	11.1	10.4
Muscle	1.2	1.0	-9
Neurological	6.2	4.9	4.3
Skin	42.3	35.7	36.7
Lymphatic	1.5	1.2	1.4
Other	8.1	7.3	7.5
No Abnormalities	23.0	29.7	30.2
Number of cases	12821	2576	69059

MOST FREQUENT DIAGNOSES BY EXPOSURE GROUP

	_	Expsoure Group		
Diagnosis	High	Low	Other	
No Diagnosis	35.1	45.1	43.9	
Skin Disease	32.1	24.4	25.4	
Mental Disorder	14.2	9.9	9.7	
Dis. of Musculoskelatal				
System	8.6	5.9	6.5	
Dis. of Sensory Organs	5.4	3.9	3.9	
Alcoholism	3.7	3.4	3.3	
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Number and Percent Distribution of Selected Malignant Neoplasm Cases Among 84,456 Veterans Recorded in the Agent Orange Registry and Comparison to a Reference Population

Primary Site	Number of Cases	Percent Dis	Percent Distribution		
(ICD)		Registry	SEER*		
Buccal Cavity and Pharynx (140-149)	46	7.9 ^a	4.5		
Digestive System (150-159)	68	11.6	12.2		
Respiratory System (160-169)	60	10.3	8.5		
Soft Tissue (171)	11	1.9	2.6		
Skin (172)**	53	9.1	11.7		
Male Genital System/Urinary System (185, 186, 187, 188,		19.2	22.1		
Lymphomas (200, 201, 202)	117	20.0ª	15.0		
Multiple Myeloma (203)	7	1.2	0.4		
Leukemia (204-208)	30	5.1	6.0		
Others and ill-defined site	s 80	13.7	17.2		
TOTAL	584	100	100		

* SEER (Surveillance Epidemiology End Results): Percent distribution of malignant neoplasm cases diagnosed in 1973-77 by primary site, aged 25-39, all races, males, and all areas excluding Puerto Rico.

** Excluding basal and squamous carcinoma

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^a The 95% confidence limits for differences in proportions do not include zero

"PREPRINT EXTENDED ABSTRACT"

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Presented Before the Division of Environmental Chemistry American Chemical Society Washington, D.C. September 1983

Evaluation of Veterans for Agent Orange Exposure

M. R. Filckerl and A. L. Young² *

IKansas City Veteran's Administration	ZAgent Orange Project Office
4801 Limwood Boulevard	Veteran's Administration
Kansas City, Hissouri 64128	Washington, D.C. 20420

The Veteran's Administration has been evaluating Vietnam veterans for signs and symptoms of adverse health effects attributable to phenoxyherbicide and dioxin exposure.

Agent Orange Registry: Preliminary data collection began as the Agent Orange Registry in 1978. Any veteran concerned about the health effects of Agent Orange could report to a Y.A. hospital for a complete medical and exposure history, physical examination, and selected laboratory tests. The names, addresses, and results of the evaluations were compiled by computer in the hopes of identifying any trends in symptomatology or health.

<u>Rationale for the Registry Exam</u>: The importance of the complete history taking from involved veterans becomes apparent upon a review of the known toxicology of the herbicides and TCDO. Veterans were being evaluated from ten to twenty years after alleged exposure; adverse health effects of 2,4-D and 2,4,5-T should manifest themselves shortly after exposure and -- as in the case of the peripheral neuropathies -- persist at most up to three years. In addition, toxic effects of TCDD are rarely present in the absence of chloracne, which itself only rarely persists up to ten to twenty years. Thus, the majority of veterans, even if heavily exposed, would be expected to have no or few residual signs or symptoms at the time of their Agent Orange evaluation.

A complete history is also essential to avoid confusing the effects of other toxins such as alcohol with those of Agent Orange, for the human body has only a finite number of responses to a large number of toxic agents.

<u>Special Features of the Agent Orange Exam</u>: In addition to the standard medical history, veterans were asked about their recollections of known herbicide and toxic chemical exposure frequency, intensity, and duration, as well as any history of neoplasia, infertility, abortion, or teratogenesis in themselves or their families.

Laboratory testing included hematologic, hepatic, and radiographic analysis. When necessary, nerve conduction studies and sperm counts were obtained.

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* A summary of current information on the Agent Orange Registry was presented by Dr. B.M. Shepard at the Symposium Presentation August 30, 1983. These data are provided in the attached narrative and seven tables.

"PREPRINT EXTENDED ABSTRACT" Presented Before the Division of Environmental Chemistry American Chemical Society Washington, D.C. September 1983

Evaluation of Veterans for Agent Orange Exposure

M. R. Flicker and A. L. Young*

Veterans Administration Medical Center 4801 Linwood Boulevard Kansas City, MO 64128 Agent Orange Projects Office Veterans Administration 810 Vermont Avenue, N.W. Washington, D.C. 20420

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Laboratory testing included hematologic, hepatic and radiographic analysis. When necessary, nerve conduction studies and sperm counts were obtained.

Summary of Known Health Effects of 2,4-D and 2,4,5-T and TCDD: In order to assess the forthcoming data from the Agent Orange registry, the following summary is relevant:

1. 2,4-D -- peripheral neuropathy (most important), neuropenia and acute gastrointestinal effects (nausea, vomitting) and headache;

* B. M. Shepard presented Tables 1-7 (attached) on August 30, 1983.

2. 2,4,5-T and TCDD -- chloracne, a form of acne often clinically indistinguishable from acne vulgaris; porphyria cutanea tarda: hyperpigmentation, hirsutism, hepatic dysfunction; asthenia: a symptom complex closely associated with depression and difficult to distinguish from the post traumatic stress disorder seen after all wars and catastrophes (headache, apathy, fatigue, sleep disturbance, anorexia and decreased learning ability). Normally expected to clear with time.

Symptoms arising for the first time months and years post exposure are probably due to an etiology other than 2,4-D and 2,4,5-T. The question of carcinogenesis, teratogenesis and mutageneis remains open; to date there is no proven association in humans.

Summary of Registry Results: Although the registry participants comprise a self-selected group, the composition of the registrants by service branch accurately reflects the relative population of that branch in Vietnam:

Army	66%
Marine Corps	20%
Air Force	78
Navy	68
Other	18

 $I_{i} \sum_{i=1}^{n} I_{i}$

To date, over 110,000 veterans have been evaluated. Approximately three quarters of them complained of symptoms of illness. These symptoms and their relative frequency are characterized below:

Symptom Category	Percent of Registered Patients
Dermatologic	40
Psychologic	25
fleadache	13
Peripheral Neuropathy	12
Asthenia	12
Gastrointestinal	12
Sexual Dysfunction	5
Other	44

Of the several thousand veterans complaining of dermatologic problems, only one may possibly turn out to be chloracne.

Many of the psychiatric/asthenic patients have been variants of the delayed stress response syndrome seen after all major wars.

Noteworthy is that the majority of the above symptoms bear no correlation to the known toxicology of Herbicide Orange; in addition, no increased incidence of malignancy have been observed in this population which, by virtue of its self-selected nature, may have been expected to exhibit artificially higher than baseline rates in the general population.

Supporting the above data is the observation by the Armed Forces Institutes of Pathology that there is no unusual clustering or incidence of tumor among the over twelve hundred pathological specimens from Vietnam veterans examined to date.

Conclusions: Thus, the Agent Orange Registry data do not support the thesis that there is any unusual long-term morbidity associated with Vietnam service or Agent Orange exposure.

COMPARISON OF DISTRIBUTION OF EXAMINEES BY BRANCH OF SERVICE WITH DISTRIBUTION IN DEPARIMENT OF DEFENSE DATA

		Percent	age In
Branch of Service	Number	AO Registry	DoD Data
Army	56594	67.0	67.2
Marines	15373	18.2	13.6
Air Force	6514	7.7	12.7
Navy	5101	6.0	6.3
Coast Guard	76	.1	.1
Other/Not. Specified	798	0.9	-
Total	84456	100	100

DISTRIBUTION OF TYPE OF EXPOSURE REPORTED BY EXAMINEES

Type of Exposure	Number	Percentage
During Actual Spraying	9453	11.2%
While handling Agent Orange	2734	3.2
While passing through defoliated area	49722	58 .9
Unsure of actual exposure	9109	10-8
Other	2855	3.4
Unspecified	10585	12.5
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Total	84456	100.0

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FIVE MOST FREQUENT COMPLAINTS

Complaint	Number	Percentage
No complaint	22645	26.8
Skin Rash	32846	38.9
Nervousness	14825	17.6
Beadaches	11874	14.1
Abdominal Complaints	10239	12.1
Personality Disorders	8614	10.2

MOST FREQUENT DIAGNOSES

Diagnosis	Number	Percentage
No Diagnosis	35957	42.68
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Mental Disorders	8783	10.4
Dis. of the Musculo-Skeletal System	5778	6.8
Dis. of the Sensory Organs	3520	4.2

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MOST FREQUENT COMPLAINTS BY BRANCH OF SERVICE (PERCENTAGES)

Complaint	Аюлу	Marines	Air Force	Navy	Coast Guard	Unknown Other
Skin rash	39.1	39.5	37.7	36.3	38.2	36.6
Nervousness	17.9	18.7	14.2	14.5	17.1	17.6
Beadaches	14.1	15.1	12.6	12.3	15.8	12.7
Abdominal complaints	12.0	13.3	11.6	10.8	21.0	8.4
Personality problems	9.9	12.1	8.8	8.9	14-5	7.5
Numbness	8.2	8 .9	8.0	8.3	10.5	7.5
Muscle aching, tingling	8.1	8.1	8.7	8.0	15.8	5.1

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MOST FREQUENT DIAGNOSES BY BRANCH OF SERVICE (PERCENTAGES)

Diagnosis	Axmy	Marines	Air Forçe	Navy	Coast Guard	Other/ Unknown
No diagnoses	42.5	42.9	41.9	43.2	35.5	46.7
Dis. skin/sub		2.205	2102	1.000	0313	
contaneous tissue	26.2	26.5	26.3	25.3	23.7	21.7
Mental disorder	10.6	11.7	7.8	8.3	13.2	7.5
Dis. of bones,						
joints, tendons	6.7	6.7	8.2	6.7	3.9	6.5
Dis. of sensory	4.2	4.3	4.1	3.9	2.6	2.8
Alcoholism	3.4	3.5	2.7	3.1	3.9	2.5

Table 7

Number and Percent Distribution of Selected Halignant Neoplasm Cases Among 84,456 Veterans Recorded in the Agent Orange Registry and Comparison to a Reference Population

Primary Site	Number of Cases	Percent Distribution		
(ICD)		Registry	SEER*	
Buccal Cavity and Pharynx (140-149)	46	7.9 ^a	4.5	
Digestive System (150-159)	68	11.6	12.2	
Respiratory System (160-169)	60	10.3	6.5	
Soft Tissue (171)	11	1.9	2.6	
Skin (172)**	53	9.1	11.7	
Male Genital System/Urinary System (185, 186, 187, 188,		19.2	22.1	
Lymphomas (200, 201, 202)	117	20-0 ^a	15.0	
Multiple Myeloma (203)	7	1.2	0.4	
Leukemia (204-208)	30	5.1	6.0	
Others and ill-defined sites	5 80	13.7	17.2	
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* SEER (Surveillance Epidemiology End Results): Percent distribution of malignant neoplasm cases diagnosed in 1973-77 by primary site, aged 25-39, all races, males, and all areas excluding Puerto Rico.

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a The 95% confidence limits for differences in proportions do not include zero