DRAFT, 5/19/78

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PUBLIC HEALTH SERVICE-CDC-ATLANTA
EPI 77-84-2 (date)

To : Director, Center for Disease Control

From : Chronic Diseases Division
Bureau of Epidemiology

Subject: Hematopoietic Abnormalities, Ridgecrest, California

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SUMMARY

Thirty-five cases of chronic leukopenia were investigated at a Navy Ordnance Test Station in China Lake, California. Although many WBC counts drifted downward over many years, no one event, procedure, or chemical exposure could be detected as common etiology. No clinically significant illnesses were reported as a result of leukopenia, but suggestive bone marrow biopsies and chronically decreasing leukocyte counts demand increased surveillance for evidence of myelosuppression and reversibility.

INTRODUCTION

In the course of investigating a leukemia cluster in the town of Ridgecrest, California, the Cancer Branch learned that some of the employees at the nearby China Lake Naval Weapons Center (CLNWC) were experiencing decreasing white blood cell counts over many years. On contacting the base infirmary, the investigation EIS officers learned that several physicists, chemists, and ordnance field workers in a variety of job descriptions and locations were found to have a dropping white blood cell count over several years. After discussion with

Clark W. Heath, Jr., M.D., Director, Chronic Diseases Division; Glyn G. Caldwell, M.D., Chief, Cancer Branch; Jim Chin, M.D., State Epidemiologist, California; Captain Bob Taylor, M.D., Chief, Medical Division, CLNWC; A. D. Wiruth, Chief, Office of Safety, CLNWC; and Paul Cuykendall, industrial hygienist, CLNWC, they decided that a detailed epidemiologic investigation was necessary. In August, 1977, Gary Stein, M.D., EIS Officer, Cancer Branch, traveled to China Lake, California, to investigate possible etiologies for the hematologic laboratory findings.

BACKGROUND AND SITE ACTIVITIES OF CHINA LAKE NAVAL WEAPONS CENTER

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The China Lake Naval Weapons Center in China Lake, California, is a huge complex of research and development facilities for ordnance testing, propulsion systems, radar/microwave installations, and electronic warfare located 100 miles east of Bakersfield, California, and 180 miles north of Los Angeles in Kern, San Bernardino, and Inyo Counties. The CLNWC covers 600 square miles east of the southern Sierra Nevada Range and west of Death Valley, but the Center's major activities take place next to the support town of Ridgecrest (population 12,500, 1970 Census--Figure 1). The China Lake Weapons Testing Center employs approximately 4,100 people, most of whom are civilians living in Ridgecrest. The Navy had previously felt that some employees warranted hematologic monitoring because of the multitude of chemical exposures and possible myelosuppression. In 1976, a chemist was given medical retirement and financial compensation for chronic exposure to ethylene oxide and its purportedly irreversible leukopenic effect. It would be important, therefore, to identify all hazardous chemical exposures and identify individual or synergistic myelotoxic sequelae.

The research and development of propulsion and ordnance systems is unique in chemistry, testing equipment, and purpose. The need for a brief introduction to activities and job descriptions, keeping in mind chemical and radiation exposures, becomes apparent. Refer to Table 1 and Figure 1.

China Lake Propulsion Laboratories (CLPL) operations are: motor assembly, propellant mixing/pressing, and computer analysis of ordnance. Typical organic solvents such as phenol, benzene and short chain alcohols are used in this area as reagents and for cleaning purposes. The propulsion laboratories also routinely handle high density hydrocarbon fuels, aviation gasoline, and RDX (hexahydro 1,3,5 trinitrostriazine) propellants with polybutadiene and isocyanate binders. Their analytic work includes ramjet ballistics, solid propulsion technology, and combustion products of ordnance weapons.

The Skyline facility includes a number of static test areas, a 40-foot drop test, bullet impact test, shaker and shock absorption tests which determine ordnance reaction kinetics in an encased rocket motor or warhead shroud. Minimal exposure to chlorinated hydrocarbons occurs in this area, but virtually no other propellant exposure.

The Salt Wells complex is a series of buildings for extensive propellant explosive and pyrotechnic research. The work includes developing electronic detonators, X-ray testing for structural defects, and thermal effects testing on weapons systems. The X-ray facility has been consistently monitored by the Nuclear Regulatory Commission for possible leakage and compliance with safety measures. Film badges and other dosimeters record the amount of gamma radiation, and present readings are within current standards. Other

activities of the Salt Wells complex include mixing, casting, pressing, and curing explosives for motors and warheads. Most of the mixing and pouring of propellants and binding systems are done by remote control with only occasional direct worker contact.

The Michelson Laboratory is a gargantuan series of chemistry, physics, electronic laser and metallurgical laboratories. A large industrial machine shop with metal lathes and a drill press for fabricating missile systems is located here as well. A third major portion of the laboratory is administrative.

The Supply Department provides all material support for the entire base with no direct chemical exposure; all containers of raw materials are tightly sealed at this point. The Public Works Department is a maintenance force of electricians, plumbers, construction, and repair teams, which permeates every area at the base, but no unusual exposures were recorded.

The Administration in area 33 includes the technical information offices and is the hub of managerial activity for the base.

The Laser lab northeast of the Michelson Laboratory uses a variety of compressed gasses for its optical etching facility but none of the ordnance chemicals previously described.

The C-T complex does small scale explosive testing. Contact with propylene oxide and ethylene oxide from slow-burning of hydrocarbon fuels requires full respiratory protective equipment. The carbonaceous materials from combustion comprise the only chemical exposure in this area.

Skytop complex is a quality assurance testing area for rocket motors and warheads; the only chlorinated hydrocarbon used in this area is 1,1,1,-trichlorethylene.

The Magazine area is used for storage of all incoming and outgoing ordnance. The aircraft facility tests aircraft survival to explosions, and the Thompson Lab is mostly for classified paperwork.

The Naval Air Facility is an on base airport; no chemical exposure occurs in this area.

jet fuel, gasoline, hydraulic fluid, etc. + noise, exhaust, heat

Supersonic Naval Ordnance Research Track (SNORT) is for dynamic testing of solid fuels via a track-sled which reaches Mach speeds.

Randsburg Wash is a highly restricted and classified area for electronics warfare and radar counter-measures. Non-ionizing microwave and radar frequencies are emitted here.

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FIVE CASE HISTORIES

These 5 exposure summaries typify routine activities, white count decrements and possible hypotheses of leukopenia etiology.

Case #1, This 50-year-old white male who had no previous major medical illness has worked in the Michelson research laboratory for 24 years as a chemist. His WBC counts ranged from 7-9,000 in the early 60's and gradually dropped to the 3-5,000 range in ten years. In 1972 he was exposed to benzidine and in June of 1974 was informed by CLNWC clinic that he had a low WBC count which was confirmed by bone marrow aspirate and biopsy. The

diagnosis was myelosuppression possibly from toxic chemical exposure. The patient remained entirely asymptomatic. He used benzidine sporadically for the next several years but his major exposures were metal perchlorates and butadiene polymers. From 1954-1972, the compounds most frequently found in his lab were benzene, toluene, hexane, cyclohexane, chloroform acetones, fluorocarbons, and freons. In 1972 the percent of his segmented neutrophils dropped from 75% to 50% ($p<.01$), but never reached an absolute segmented neutrophil count <1000 cells/cc.

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Case #2. This 60-year-old white female Ph.D. chemist with over 20 years laboratory experience was well until 1962 when she developed recurrent respiratory infection, headaches, and eye irritation. In 1972 she was noted to be leukopenic with complaints of chronic fatigue and severe headaches. She also has a history of multiple drug ingestion and chronic exposure to herbicides. Physical exam revealed no significant lymphadenopathy, or hepatosplenomegaly, and she had no evidence of immune inhibitors of hematopoiesis by culture of her bone marrow. She was given medical retirement from "possible exposure to myelotixic compounds", including polyurethanes, and benzene derivatives.

Case #3. The third case is a 43-year-old white male materials engineer who worked in a chemistry lab for 8 years with benzene, ethylene oxide, trichlorethylene, cadmium, and mercury, but has had a desk job for the past 4 years. He has been entirely asymptomatic, but has shown an overall drop in white count since 1957. His lowest count was 2.7 in 1974 unaccompanied by change in work habits or known chemical exposure. He has never experienced

an absolute granulocytopenia. A bone marrow examination revealed mild hypoplasia in the myeloid series and reversibility indeterminate from 1 marrow exam.

Case #4 (Figure 2). This is a 58-year-old chemist who was given compensated medical retirement from CLNWC after chronic exposure to propylene and ethylene dioxide which began in 1969. His drop in white count was not detected until 1972 when it remained consistently low and he was retired soon thereafter. No notable increase in WBC values occurred after a few months away from ethylene oxide in 1973. A bone marrow biopsy revealed a mild myelosuppressive picture. The patient remains in good health and has not experienced increased susceptibility to clinical infection.

Case #5. The fifth case is a 54-year-old black male who has worked at CLNWC since 1960 as a research chemist. He has had chronic but not excessive exposure to common organic solvents. From 1963 until 1969 he worked with lead sulfide, thiourea, trichlorethane, methyl ethyl ketone, and occasionally toluene and benzene. In 1970 he changed projects and his major exposures were various acids, sodium hydroxide, and silane gas. He has never been involved with propellants or explosives. A bone marrow study done in May 1971 showed a maturation arrest of the myeloid series at the myelocytic level. He has remained asymptomatic and has not experienced clinical signs of illness or increased susceptibility to bacterial infection.

Case Definition

A case of leukpoenia was identified when an employee had 1 white count equal to or less than 4.3 X 10^3 WBC's/cc whole blood or 2 WBC counts equal to or below 4.5 with previous routine counts documents above 7,500 white cells per cubic centimeter. It is extremely difficult to define leukopenia

white counts vary diurnally and demarginate from blood vessel walls readily in response to small increases in catecholamine levels (1). Many antibiotics, antihistamines, steroids, and tranquilizers are known to alter white counts and, of course, bacterial and viral infections can rapidly raise or lower a white blood count temporarily. It is unclear whether age or race affect white counts, as reports are conflicting (2,3,4).

INVESTIGATIVE METHODS

The investigation required several approaches. First, the cases of possible leukopenia were interviewed to obtain detailed occupational histories, known toxic chemical exposures, and adequacy of specific work site protective measures. Next, the cases were asked about radiation exposure, infectious disease frequency, and any hematologic disorders they may have experienced. Exposure to drugs known to lower WBC counts was also obtained. The response to these questions was tabulated to focus on any particular possible common cause of the leukopenia.

The next source of information came from each monitored employee's white count graph over time. Date of white count drop(s) were noted and compared to that individual's exposure history to determine if possible which of the numerous chemical exposures may have played a role in that person's shifting white counts.

Another approach defining more subtle group differences in leukocyte counts was to obtain 1 WBC count on each worker in a suspect code or area and compare that group data with the Health and Nutrition Examination Survey-I (HANES-I) data for white cell count frequency distributions. These data consist of age, sex, and race, specific hematologic parameters including white blood cell counts and differentials.

The white blood cell counts done at the CLNWC medical center were drawn between 0800 and 1000 and run on a "Hycel Counter 300" with Dade CH-60 Hematology Controls. The HANES-I hematology data was obtained on a "Coulter Model Fn" counter using Coulter 4C cell suspension as standard and control.

To eliminate time of specimen collection and variability of electronic counters, the firemen of the public works division were chosen as an unexposed "on-base" control group. These 2 standards were used to compare white counts in 19 different groups of workers in a variety of locations and exposures on the ordnance testing base.

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RESULTS

Table 2 lists the age, sex, workplace, job title, and lowest white count of the 34 cases of possible leukopenia. The workplaces described are separated by miles of desert as seen by reading Table 2 and Figure 1. Most of the possible leukopenia cases are centered in the Michelson research, Salt Wells, and CLPL areas. Forty-two percent of the possible cases are either chemists or physicians, but 16 other job categories with leukopenia make 1 work area or job unlikely as a cause of the low white blood counts (Table 3).

The 35 cases of leukopenia have no detectable universal similarity in reported chemical exposure or drug history. Table 4 lists compounds used in explosives/propellants wetting by hematologic effect and the percentage of leukopenia cases reporting exposure to the agent. Of the compounds known to suppress white counts, benzene exposure was reported in 28% of the workers and benzene or benzene derivative was reported in 45% of chemical exposure history.

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Only 1 person with leukopenia felt that exposure to toxic compounds had resulted in increased frequency of illness; no one reported other hematologic disorders or previous sensitivity to any of the drugs known to lower white counts (Table 5).

Eighty-eight percent (31/35) of the leukopenia cases had their lowest recorded white count from 1975-77 with approximately equal distribution in the latter two years (Figure 3). The remaining 4 had their lowest counts in the years 1972-74. It is difficult to tell exactly at which point leukopenia exists because the insulting agent may have been present for weeks or months before a low white blood cell count was detected. The increase in cases of leukopenia in 1976-77 may be due to increased surveillance activities.

White counts screening results (Table 6) show engineering services, engineering prototypes, chemistry, and counter-measures divisions significantly different from HANES-I frequency distributions (Figure 4). The latter division was higher than expected normals without absolute lymphocytosis as sometimes reported with non-ionizing radiation (5). Although other divisions had employees who were considered possibly leukopenic, the group data of WBC counts indicated that they did not significantly vary from HANES-I normal values. The white counts of the fire fighting division were compared to the other divisions and several groups were found to be significantly different from the firemen's WBC distribution. The engineering services, engineering prototype and counter-measures varied in the same direction as they had from HAMES-I data. Why the chemists were not statistically different from the firemen, but were statistically lower than HANES-I, in unclear. The "on-base" control was an attempt to eliminate counting procedure (type of counter, time

of day, technicians) differences, but it appears to have created more differences. The small number of individuals (94) used as the standard may account for the huge difference because white counts have sizeable inherent oscillations, and the HANES-I data (N=6444) may have dampened the inherent flux (Figure 5).

CONCLUSIONS AND DISCUSSION

From analysis of 35 cases of possible leukopenia, no particular work-site, job category, or toxic agent could universally account for the chronically depressed white counts. Good work habits, adequate hoods, and ventilation systems make laboratory accidents or poor hygiene an unlikely cause for any undue myelotoxic exposure.

Forty-five percent of the chemical exposure histories include benzene or a derivative, an established myelotoxin and leukemogen.

Undue ionizing radiation exposure is unlikely because the base maintains strict adherence to Nuclear Regulatory Commission standards. Non-ionizing radiation is also an unlikely cause of leukopenia as the only source of this electromagnetic frequency is 20 miles from any possible leukopenia case and none of the counter-measures (radar) division employees show any leukopenic effect. They, in fact, vary to the high side of normal distributions.

One hypothesis is that some of the less commonly used chemicals have a synergistic myelotoxic effect, but when they are examined individually show no compromising ability. If this were superimposed on aromatic (benzene) derivative exposure, it may account for the leukopenic trend. The individuals without any chemical exposure may be normal variants and add to the differences found in the grouped data.

Only 1 employee noted an increased frequency of clinical illness due to toxic chemical exposure, but it is unclear whether this exposure occurred at work or home. No other employees noted any unusual illnesses or clinically significant changes from the laboratory findings presented here.

There is obvious room for further studies with more stringent controls.

RECOMMENDATIONS

1. The base-wide surveillance system to pick up possible leukopenia cases should be expanded to include all employees annually.

2. All blood specimens for WBC determination should be collected within the same 2- or 3-hour time period every time they are run to eliminate circadian flux.

3. The employee should be at rest when blood for WBC count is collected.

4. When a case of possible leukopenia is detected, all employees in that division should be tested for WBC counts quarterly to a) pick up other possible cases, b) delineate base-wide trends.

5. If a possible case of leukopenia reveals a WBC count $<4.3 \times 10^3$ cells/cc whole blood on 3 separate occasions separated by 1 month intervals, that employees and supervisors should make every effort to remove any myelotoxic agents from the worksite.

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6. If possible leukopenia persists, a bone marrow exam should be performed at least annually until a hematologist documents acceptable production of the myeloid series.

7. Removing an employee from worksite is acceptable only as a short-term measure to allow time for discovery of the myelosuppressive agent.

8. Routine hood and ventilation systems in all laboratories should be vigorously maintained.

9. The power field intensity data for non-ionizing radiation in each workplace should be made available to employees of that site.

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TABLE 1

DISTRIBUTION OF LEUKOPENIA CASES BY WORK LOCATION

AT CHINA LAKE NAVAL WEAPONS CENTER

AUGUST 1977

Code	Activities	No. Employees	No. Leukopenia	No. Leukopenias per 100 employees
32	CLPL ("Clip")	129	3	2.3
32	Skyline	15	0	0
32	Salt Wells	131	5	3.8
33	Michaelson-Research Lab	1,041	25	2.4
33	Supply Dept.	106	0	0
33	Public Works Dept.	557	0	0
33	Administration	831	1	0.12
33	Laser Lab	104	0	0
34	Uninhabited	0	0	0
35	C-T Complex	7	1	14.3
35	Skytop Complex	31	1	3.2
36	Magazines, Aircraft; Thompson Lab	397	0	0
37	Naval Air Facility	431	0	0
38	SNORT	33	0	0
39-44	Test Ranges	0	0	0
31	Randsburg, Wash.	130	0	0
All areas		4,143	35	.82

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Table 2

Case	Age	Sex	Workplace	Date of Lowest WBC Count	Lowest WBC	Job Description
1	43	M	Mich-Res	9/74	2.7	Materials Eng.
2	55	F	Salt Wells	2/77	3.0	Res. Chem.
3	50	M	Mich-Res	8/73	3.0	Res. Chem.
4	39	M	Mich-Res	7/77	3.1	Phys. Sci. Admin.
5	32	M	Admin Bldg	2/77	3.2	Mech. Eng.
6	43	M	Mich-Res	10/76	3.2	Metallurgist
7	45	M	Skytop	2/77	3.2	Mech. Eng.
8	58	M	Salt Wells	2/72	3.3	Chemist
9	37	M	Clip	3/76	3.4	Res. Chem.
10	34	M	Salt Wells	10/74	3.5	Chem. Eng.
11	49	M	Mich-Res	4/77	3.5	Res. Phy.
12	50	M	Mich-Res	9/76	3.6	Materials Res. Engineer
13	52	M	CT4	1/76	3.9	Technician
14	60	M	Mich-Res	(8/77)	4.0	Mech. Eng. Tech.
15	40	M	Mich-Res	10/76	4.0	Phys.
16	63	F	Mich-Res	11/75	4.0	Photographer
17	64	M	Mich-Res	6/76	4.0	Phys. Sci. Tech.
18	48	M	Salt Wells	10/76	4.0	Physicist
19	64	M	Mich-Res	3/77	4.1	Chemist
20	38	F	Mich-Res	6/77	4.1	Chemist
21	51	M	Mich-Res	12/75	4.2	Artillery repair
22	34	M	Mich-Res	9/75	4.2	Physicist Supvr
23	43	M	Clip	4/76	4.2	Chem. Eng.

Table 2, Continued

Case	Age	Sex	Workplace	Date of Lowest WBC Count	Lowest WBC	Job Description
24	52	M	Mich-Res	3/77	4.2	Chem. Supvr.
25	46	M	Mich-Res	12/76	4.3	Technician
26	47	M	Mich-Res	6/75	4.3	Chemist
27	40	M	Mich-Res	7/76	4.3	Gen. Engineer
28	51	M	Mich-Res	7/76	4.3	Plastics Eng.
29	48	M	Mich-Res	10/76	4.3	Chemist
30	45	M	Clip	5/76	4.3	Mech. Eng. Tech.
31	35	M	Salt Wells/Clip	1/77	4.3	Explosives Operator
32	38	M	Mich-Res	4/77	4.4	Etched Circuit Maker
33	64	M	Mich-Res	4/77	4.5	Oiler
34	46	M	Mich-Res	6/76	4.5	Chemist
35	54	M	Mich-Res	2/77	4.5	Chemist

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Table 3

Leukopenia by Job Category
at Naval Weapons Center

Job Category	No. of Workers	Percent
Research Chemist	11	31.4
Research Physicist	4	11.4
Chemical Engineer	2	5.7
Mechanical Engineer	2	5.7
Engineering Technician	2	5.7
Mechanical Engineering Technician	2	5.7
Materials Engineer	1	2.8
Metallurgy	1	2.8
Materials Research Engineer	1	2.8
Explosives	1	2.8
Physical Science Administrator	1	2.8
Photographer	1	2.8
Physical Science Technician	1	2.8
Artillary Repair	1	2.8
Materials Engineer Plastics	1	2.8
General Engineer	1	2.8
Oiler	1	2.8
Etched Circuit Maker	1	2.8
	35	100%

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TABLE 4

Compounds used in Explosives/Propellant Development

with Known Adverse Physiologic Effect

	Cases Reporting Exposure	
	N	90
Leukopenic		
Benzene	10	28
Ethyl Benzene	4	11
Chlorobenzene	2	6
Chloronaphthalene	2	6
Methylcyclohexanol		0
Styrene		0
Dinitro Orthocresol		0
Myelotoxic and Leukopenic		
Benzene	10	28
Aniline		0
Myelotoxic Not Leukopenic		
Dimethylhydrazine	8	23
Hydrazine	6	17
Nitroglycerol	5	14
Nitrobenzene	4	11
Dinitrobenzene	3	6
Trinitrotolvene	2	3
Dichlorohydrin	0	0

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Other Compounds used but not Myelotoxic (usually affecting CNS, liver, kidney, or skin)

	Cases Reporting Exposure	
	N	90
Alcohols	13	37
Acids, weak	12	34
Methyl Ethyl Ketone	11	31
RDX (trinitrostriazine)	10	28
Ammonium Picrate	9	26
Acids, strong	8	23
Acetone	7	20
Xylene	7	20
Long Hydrocarbons	7	20
Toluene	6	17
Ammonium Perchlorate	5	14
Polybutadiene	5	14
Boron Hydride	4	11
Phthalates	4	11
Ammonia	4	11
Borazine	4	11
Trichlorethylene	4	11
Perchlorates	4	11
$Ca\ CO_3$	4	11
Amylene	3	9
Hydrogen Peroxide	3	9

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Table 4, Continued

	Cases Reporting Exposure	
	N	90
Mercaptans/Thiols	3	9
Methyl Ether	3	9
Pyridines	3	9
Chromium Solutions	3	9
Cyanide	3	9
Chelating Agents	3	9
Short Hydrocarbons	3	9
Aluminum	2	6
Mercury	2	6
Antimony Trisulfide	2	6
Resorcinol	1	3
Thiokol	1	3
Magnesium	1	3
Lead Azide	1	3
Camphor	0	0

Table 5

Known Leukopenogenic Agents and Percent Reported Exposure/ Ingestion Among Possible Leukopenia Cases CLNWC

	Reporting Any Exposure/Ingestion	
	No.	Percent
Antihistamines	4	11
Urethane	2	6
Nonionizing Radiation	2	6
Ionizing Radiation	1	3
Folic Acid Antagonists	1	3
Nitrogen Mustards	0	0
Periwinkle Alkaloids	0	0
Colchicine	0	0
Aminopyrine	0	0
Sulfonamides	0	0
Antithyroid Drugs	0	0
Tranquilizers, Major	0	0
Anticonvulsants	0	0

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Table 6

White Blood Cell Count Frequency Distribution Comparison

CODE	N	Work Division	HANES-I Comparison P Value	Fireman Comparison P Value
361	69	Engineering Services	<0.001	.002
364	107	Engineering Prototype	<0.001	<.001
355	94	Countermeasures (radar)	0.001	<.001
385	42	Chemistry	<0.001	NS
381	37	Physics	NS	NS
242	95	Public Works - Firemen	NS	—
264	41	Maintenance Utilities	NS	<.001
312	7	Aircraft Armament	NS	NS
3184/355	8	Electro-mechanical	NS	NS
388	22	Aerothermochemistry	NS	NS
394	21	Electro-optics	NS	NS
621	66	Quality Assurance	NS	.002
235	27	Photographic	NS	NS
324	43	Advanced Technology	NS	<.001
325	37	Engineering	NS	NS
326	66	Conventional Weapcns	NS	<.001
327	46	Propulsion	NS	<.001
337	13	Design Fabrication	NS	NS
352	17	Radio Frequency Development	NS	NS

d.f. = 26

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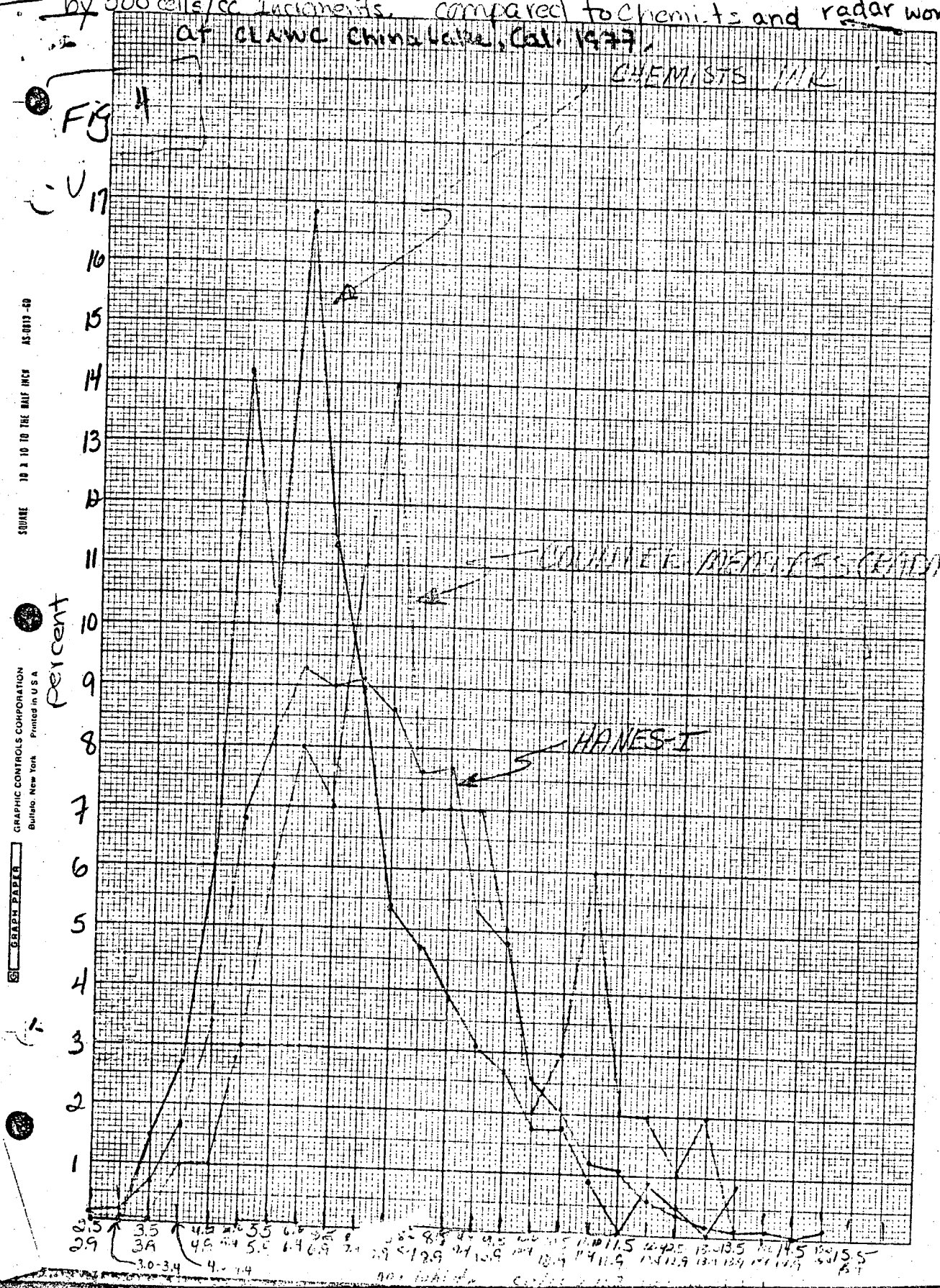
HANES-I WBC count frequency distribution in Adult Males 15-75
by 500 cells/cc Increments. compared to Chemists and radar wor
at CLAWC China Lake, Calif. 1977.

FIG 4



Ham I. WRC counts v distn data Adult Males 15-75

by 500 cells/cc WB increments

	#	% →
2.5 - 2.9	5	0.1
3.0 3.4	18	0.2
3.5 3.9	50	0.7
4.0 4.4	116	1.7
4.5 4.9	245	3.4
5.0 5.4	480	6.8
5.5 5.9	581	8.2
6.0 6.4	666	9.3
6.5 6.9	634	9.0
7.0 7.4	643	9.1
7.5 7.9	614	8.6
8.0 8.4	537	7.6
8.5 8.9	559	7.7
9.0 9.4	370	5.3
9.5 9.9	344	4.8
10.0 10.4	122	2.6
10.5 10.9	147	2.1
11.0 11.4	80	1.2
11.5 11.9	74	1.1
12.0 12.4	41	0.6
12.5 12.9	36	0.4
13.0 13.4	17	0.2
13.5 13.9	15	0.2
14.0 14.4	14	0.2
14.5 14.9	9	0.0
15.0 15.4	23	0.2 ??
≥15.5		

median 7.2 S.D. 2.36

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DATA POINTS FOR GRAPH (NOT FOR inclusion in EPI-2 as TABLE)

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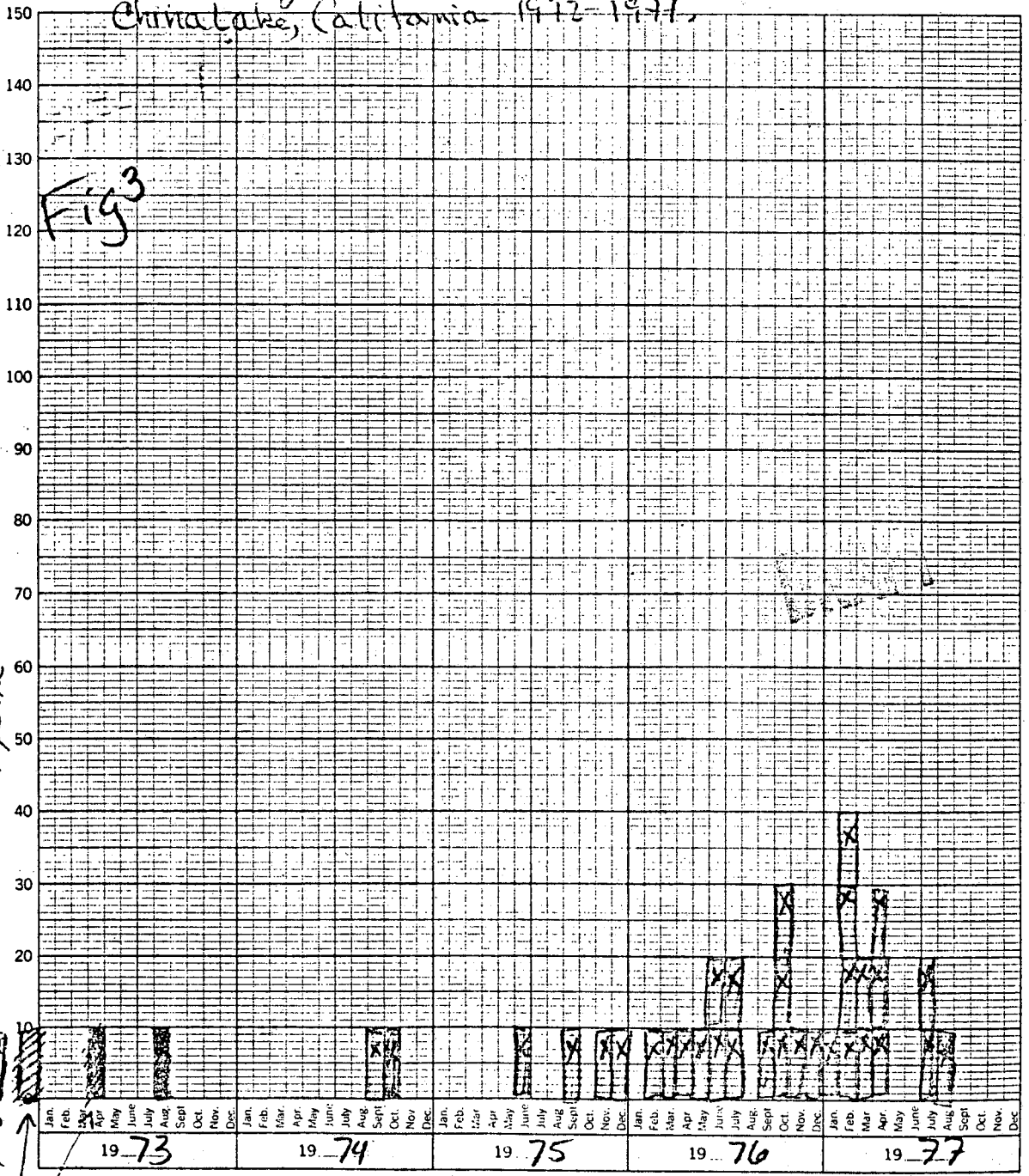
lowest white blood cell count in 35 cases of leukopenia at CLNWC

China Lake, California 1972-1977.



46 3410

K·E 5 YEARS BY MONTHS X 150 DIVISIONS KEUFFEL & ESSER CO MADE IN U.S.A.

72 28

omit

Graph 1

(no distinction from red & black)

N = 35

1 case X

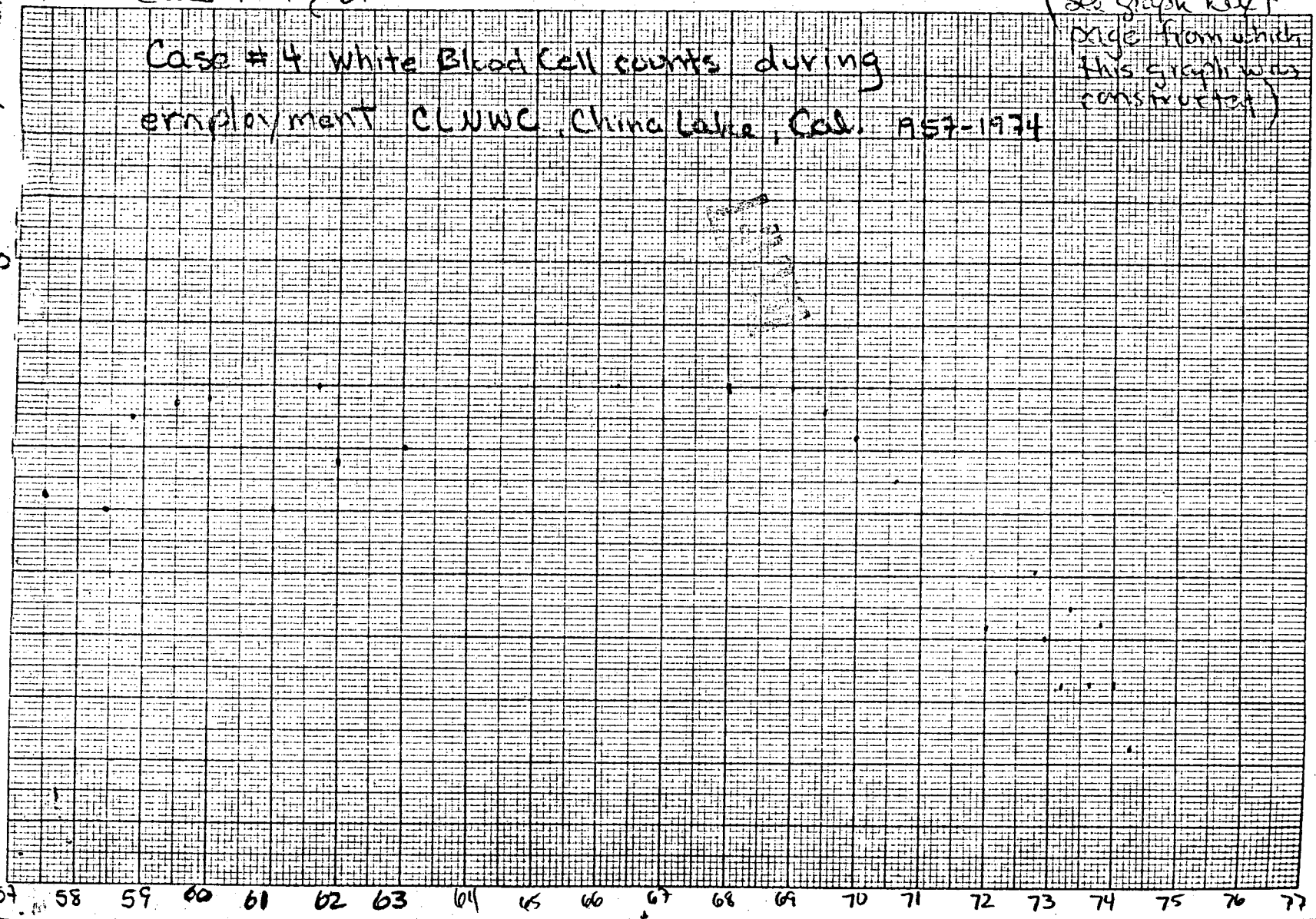
Frequency distribution of WBC counts, CLNWC
China Lake, Cal. 1977.

Fig 5

Chas Fatterman

GRAPH PAPER GRAPHIC CONTROLS CORPORATION Buffalo, New York Printed in U.S.A. SQUARE 10 X 10 TO THE HALF INCH AS-0813-GD

Case 4 Fig 2



(See graph next page from which this graph was constructed)

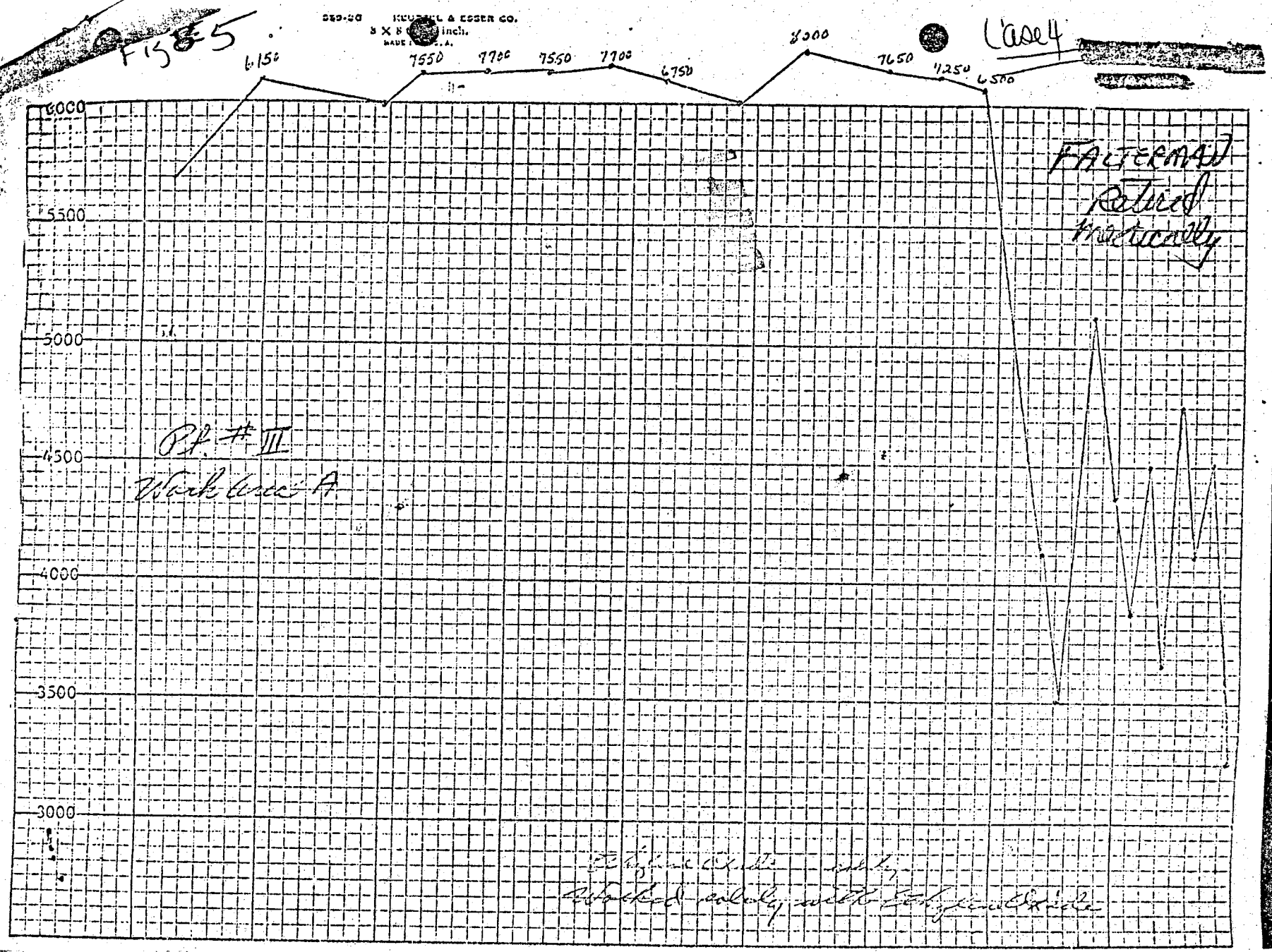
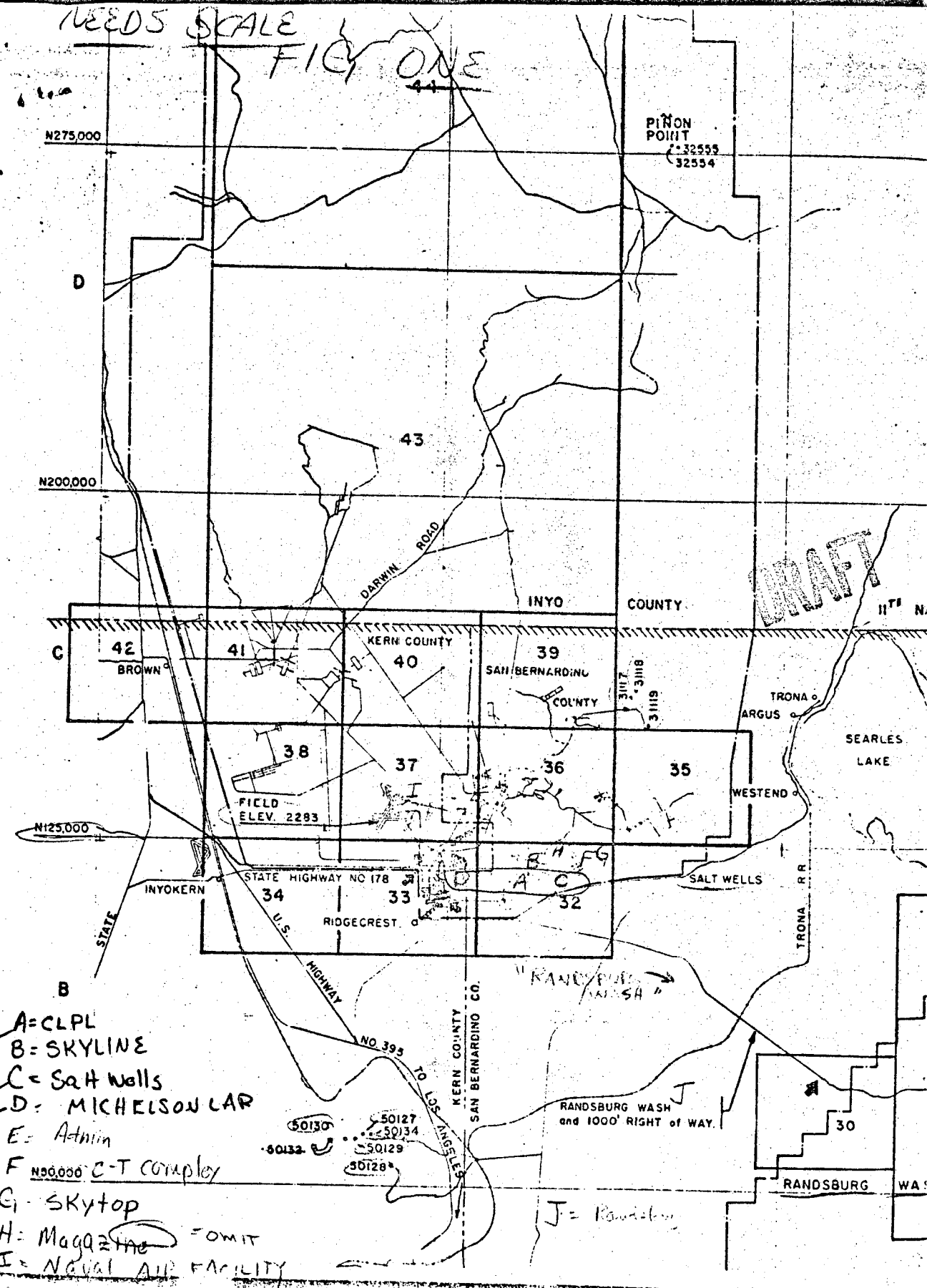


Fig 5
Case 4
6150
7550
7700
7550
7700
6750
8000
7650
7250
6500
6000
5500
5000
4500
4000
3500
3000
FALTERMAN
Retired
Medically
Pt. # III
Work Area A
Worked solely with Ethylene Oxide

NEEDS SCALE
FIG ONE



A = CLPL
B = SKYLINE
C = Salt Wells
D = MICHELSON LAB
E = Admin
F N90,000 C-T Complex
G = Skytop
H = Magazine - OMIT
I = Naval Air FACILITY
J = Randsburg

DRAFT, 6/7/78

Childhood Leukemia in Ridgecrest, California

SUMMARY

During a 5-year period from 1972 through 1977, 6 cases of leukemia were diagnosed in residents under age 19 in Ridgecrest, California. No cases of childhood leukemia had been diagnosed in Ridgecrest residents for the previous 10 years. Only very limited indirect interpersonal contact could be made for 2 of the cases, both of whom attended the same high school for a 4-month period. One of the diagnoses was made at the beginning of this period; the other was made 23 months later. Although the significance of this contact is uncertain, no other religious, social, or educational temporo-spatial relationships could be described among the cases.

INTRODUCTION

In January 1974, Stephen A. Feig, M.D., Assistant Professor of Pediatrics, Division of Hematology Oncology, UCLA School of Medicine, contacted Clark W. Heath, Jr., M.D., Director, Chronic Diseases Division, concerning a leukemia cluster he had identified in Ridgecrest, California. Subsequent communication with pediatrician Peter Pinto, M.D., Drummond Medical Group, Ridgecrest, California; Glyn G. Caldwell, M.D., Chief, Cancer Branch, Chronic Diseases Division; and Peter Falk, M.D., Division of Hematology and Oncology at UCLA, revealed a total of 6 cases of childhood leukemia in the Ridgecrest area had been diagnosed since 1972. A concern developed

Childhood Leukemia in Ridgecrest, CA

over a possible relationship between the leukemia cluster in Ridgecrest and some cases of chronic leukopenia in civilians working at the China Lake Naval Weapons Testing Center (CLNWC), adjacent to Ridgecrest. Victor Randolph, M.D., followed by Coleman Carter, M.D., EIS Officers, in the Cancer Branch, CDD, BE, began the epidemiologic investigation, and Gary Stein, M.D., Cancer Branch, traveled to Ridgecrest, California, August 11 to interview the parents and explore the clustering further.

BACKGROUND

Ridgecrest, California, population 12,500, is located in Northeast Kern County approximately 90 miles east of Bakersfield and 130 miles north of Los Angeles, where it supports the China Lake Naval Weapons Center. The Weapons Center develops and tests jet and rocket propellants as well as ordnance weapons for ballistic missiles. Most of the people living in Ridgecrest are in some way connected to base activities or its ancillary support. Ridgecrest has 4 elementary schools, 2 high schools, and 10 churches. Parental concern that some environmental leukemogen originated from the Weapons Center was fueled when it was discovered that some employees at the Navy base had other hematopoietic abnormalities (see EPI 77-___-2, Leukopenia, China Lake, California).

Methods of Investigation

The local pediatricians were canvassed for all cases of childhood leukemia for the past 10 years. Kern County death certificates were

EIS DRE

obtained and reviewed for the years 1964-1974 to identify additional cases or evidence of even earlier clustering. The families of the 6 cases whose diagnoses were made between 1972-1977 were extensively interviewed for evidence of interpersonal contact, unusual events, or exposures that could possibly help explain the cluster.

Comparison of Observed to Expected Incidence

In Ridgecrest and China Lake, a total of 6 cases of leukemia were diagnosed between January 1972 through December 1976 (Table 1). The first 3 cases were acute myeloblastic leukemia (AML) and diagnosed 6 months apart beginning September 1972. The last 3 were acute lymphoblastic leukemia (ALL); cases 4 and 5 continued the 6-8 month interval between diagnoses (Figure 2).

The expected incidence of all childhood (0-19) leukemias in the Ridgecrest/China Lake area is .27 cases annually or 1.35 cases every 5 years (1) (Table 2). The observed rate for the time period considered (January 1972-December 1976) was 4.42 times those expected. However, a leukemia case deficit existed in the 10 years prior to 1972, where 2-1/2 cases of childhood leukemia were expected in the Ridgecrest/China Lake area, yet none occurred. By coupling these time periods, the expected rate is 4 cases which lowers the observed to expected ratio from 4.42 to 1.50.

Two other childhood cancer cases occurred in this isolated population. In September 1973, a petrous bone tumor was diagnosed in a 9-year-old male and in July 1974 an epidermoid carcinoma was diagnosed in an 18-year-old male. These 2 cases were omitted from the leukemia cluster study, however.

Case #1

This 8-year-old white female presented in September 1972 with a 2-month history of malaise and anorexia with fever. After the diagnosis of AML was made by bone marrow biopsy, she developed a macular brown rash over her entire body plus numerous bruises and multiple petechiae. A remission was successfully induced with chemotherapy and she remained in remission until September 1973 when repeated attempted at re-induction with Daunomycin* (*add manufacturers disclaimer)
failed and she sustained a 2-month hospitalization with several infections and multiple platelet and red cell transfusions. Because of her extended hospital course with temporary general improvement, she was allowed a week-end leave. Subsequently she was found weak and stuporous at home, and was moribund when rushed from Ridgecrest to UCLA hospital.

Case #2

This previously healthy 7-year-old white male developed general malaise, "nasal stuffiness," and a left earache unaccompanied by fever or headache in March 1973. His left tympanic membrane subsequently perforated and he

developed left-sided proptosis and severe back pain. After noting a peripheral white count of 27,000, a bone marrow biopsy confirmed the diagnosis of AML. He was held in remission with chemotherapy over the summer, but relapsed in October even after receiving intrathecal methotrexate and CNS irradiation. He developed uncontrollable skin infections on both hands and buttocks. He was given more chemotherapy, but died in escherichia coli septic shock early in the reinductive attempt.

Case #3

This 9-year-old white male was in good health until June 1973 when his parents noted increasing irritability and sporadic enuresis. He was treated for iron deficiency anemia, but developed easy bruising and poor wound healing. Epistaxis and axillary lymphadenopathy suggested a leukemic process which was confirmed by blasts in the peripheral blood smear and confirmed by bone marrow examination which also showed in some cells (Auer rods?). He received chemotherapy and remained in remission with only minor infections until November 1974 when recurrent sepsis from deep carious lesions required multiple antibiotics and continuous hospitalization. He underwent bone marrow transplant, but subsequent hepatic dysfunction and severe diarrhea and non-functioning kidneys precluded his recovery.

Case #4

This 3-year-old white female with no previous illness presented in April 1977 with a 3-day history of fever, anorexia, and leg pains. A

peripheral blood smear suggested and bone marrow biopsy confirmed the daignosis of ALL. She was immediately given vincristine and prenisone, but responded in 24 hours with hypothermia, mottled extremities, thready pulse, and grunting respirations. She was placed on a respirator but rapidly deteriorated with successive cardiac arrests and expired from cardiovascular collapse and septicemic shock.

Case #5

This 18-year-old white male presented with night sweats, sternal tenderness, frequent bruising, and cervical lymphadenopathy in December 1974. After a CBC showed a white count of 42,000 with numerous blasts, a bone marrow confirmed the diagnosis of ALL. He underwent chemotherapy with CNS irradiation, which resulted in remission by late spring. His course was complicated by an epidural leukemic infiltrate compression of the cord at T10 requiring emergency laminectomy. Chemotherapy and radiotherapy was continued, but in July 1976 he incurred widespread infectious complications including an appendiceal abscess and bilateral pleural infiltrates from which he never recovered.

Case #6

This 17-year-old white male had been in good health until November 1976 when he felt very tired and had episodes of shaking chills without fever. He also developed severe jaw pain accentuated by chewing. A CBC, which was initially confused with mononucleosis, showed a leukocytosis of 35,000

cells, 65% of which were immature lymphoblasts. He received intravenous and intrathecal chemotheraphy along with CNS irradiation which put him in remission until October 1977 when a blast crisis developed and he refused further therapy. A spontaneous unrelenting nosebleed secondary to severe thrombocytopenia and right-sided pneumonitis resulted in death in early November 1977.

Epidemiologic Features

There was concern that some leukemogen originating on the Naval Weapons base was associated with this cluster. None of the cases' parents worked in areas of the base with toxic chemical exposure nor did they ever become suspected leukopenia cases.

Four of the cases were in males; 2 were in females. Their age distribution alone made a significant degree of school or social contact unlikely. The youngest, case 4, was 3 years old and lived only 3 days after the diagnosis was made. Her father works as a mechanical engineer at CLNWC. She had no known contact with any of the other cases.

Case 2 was 7 years old; his father is a graphics illustrator and has exposure to alcoholic and some phenolic solvents. His mother works at the Naval Air Facility at CLNWC and denies chemical or radiation exposure.

Case 1 was 8 years old. The parents had no toxic exposure at employment but did have their house exterminated several times. Their healthy cat was tested and found negative for feline leukemia virus. Case 3 was 9 years old his father is an engineer at CLNWC without known occupational toxic exposure. Although he neither knew nor contacted any other of the leukemia patients, his best friend was the boy who developed petrous ridge bone cancer.

Fig DH9

Case 5 was an 18-year-old tennis player, who enjoyed hiking in the back country and worked in a filling station. His father is an electrical engineer at CLNWC but denies chemical or radiation exposure.

Case 6 was a 17-year-old student whose father was a computer programmer at CLNWC and whose mother worked at the base's photographic development lab.

Two of the cases (5 and 6) attended Borroughs High School for a 4-month period in Ridgecrest, but they were in different grades and attended no classes together. The diagnosis of case 5 was made at the beginning of this 4-month period; the diagnosis of his indirect school contact (case 6) was made 23 months later. None of the cases had any church or social contact. None of the 6 had previous hematologic problems or evidence of familial leukemia. None of the cases had ever been around sick animals or had extensive contact with wild animals. Their diets, source of drinking water, sewage treatment, or soil content contained nothing suspicious which would associate the cluster with an environmental leukemogen.

Statistical Assessment

How unusual is it to find a leukemia cluster like the one in Ridgecrest? Assuming the 1970 U.S. population in the 0-19 age bracket to be approximately 65,000,000, there would be 8,421 subsets the size of the Ridgecrest children population (7,718). Using the Poisson distribution when the expected number of cases in the community is 1.3 in a 5-year period, the probability of

observing 6 cases is 0.0125 for each subset. One could then predict that 106 case clusters could occur in these estimated subset populations for a 5-year period.

Comment

Time-space cancer clusters appear sporadically; they are always cause for concern, particularly in younger age groups. Another recent leukemia cluster in Rutherford, New Jersey, has yet to reveal common environmental or genetic risk factors to interweave the cases (2), latent periods between individual carcinogenic exposure and appearance of a cluster can range from 2-20 years or greater, making it extremely difficult to pinpoint common factors among the cases. Nonetheless, clustering requires epidemiologic scrutiny to generate new hypotheses for the origins of human cancer.

Fig One

REFERENCES

1. Third National Cancer Survey: Incidence Data. DHEW Pub No NIH 75-787, March 1975

2. MMWR 27:15, 1978

TABLE 1

Leukemia Cases, Age 0-19, Ridgecrest, California

January 1972 - December 1976

Case	Race Sex	Age at Diagnosis	Month and year of Onset	Diagnosis	Death	Diagnosis
1	WF	8	9/72	9/72	11/73	AML
2	WM	7	3/73	3/73	11/73	AML
3	WM	9	8/73	10/73	3/75	AML
4	WF	3	4/74	4/74	4/74	ALL
5	WM	18	8/74	2/75	7/76	ALL
6	WM	17	11/76	12/76	9/77	ALL

AML = acute myeloblastic leukemia

ALL = acute lymphoblastic leukemia

Table 2

Incidence of Leukemia in Ridgecrest and China Lake, California

1972-1975

Age Group	Population	Annual Expected Incidence	Annual Expected Number	5-Year Observed
0- 4	1734	6.6	0.114	1
5- 9	2135	3.1	0.066	3
10-14	2215	2.5	0.055	0
15-19	1634	2.2	0.036	2
	7718	14.4	.271	6

$\frac{\text{Obs}}{\text{Exp}} = 4.42$

Fig One

This map should be used to show boundaries of China Lake and Ridgecrest & relative positions of cases of Leukemia by number (include where naval ordnance center is)

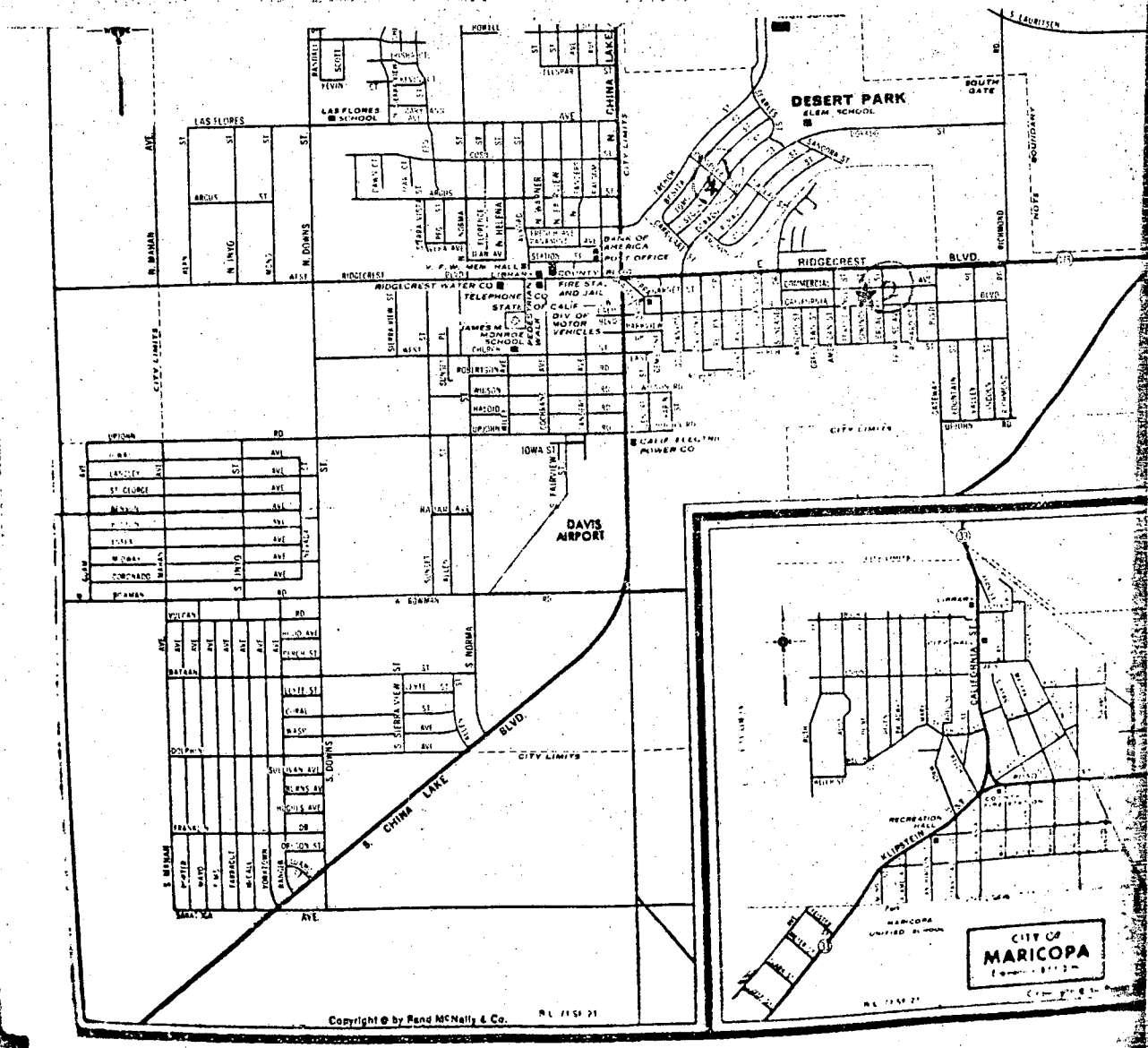


Fig Due

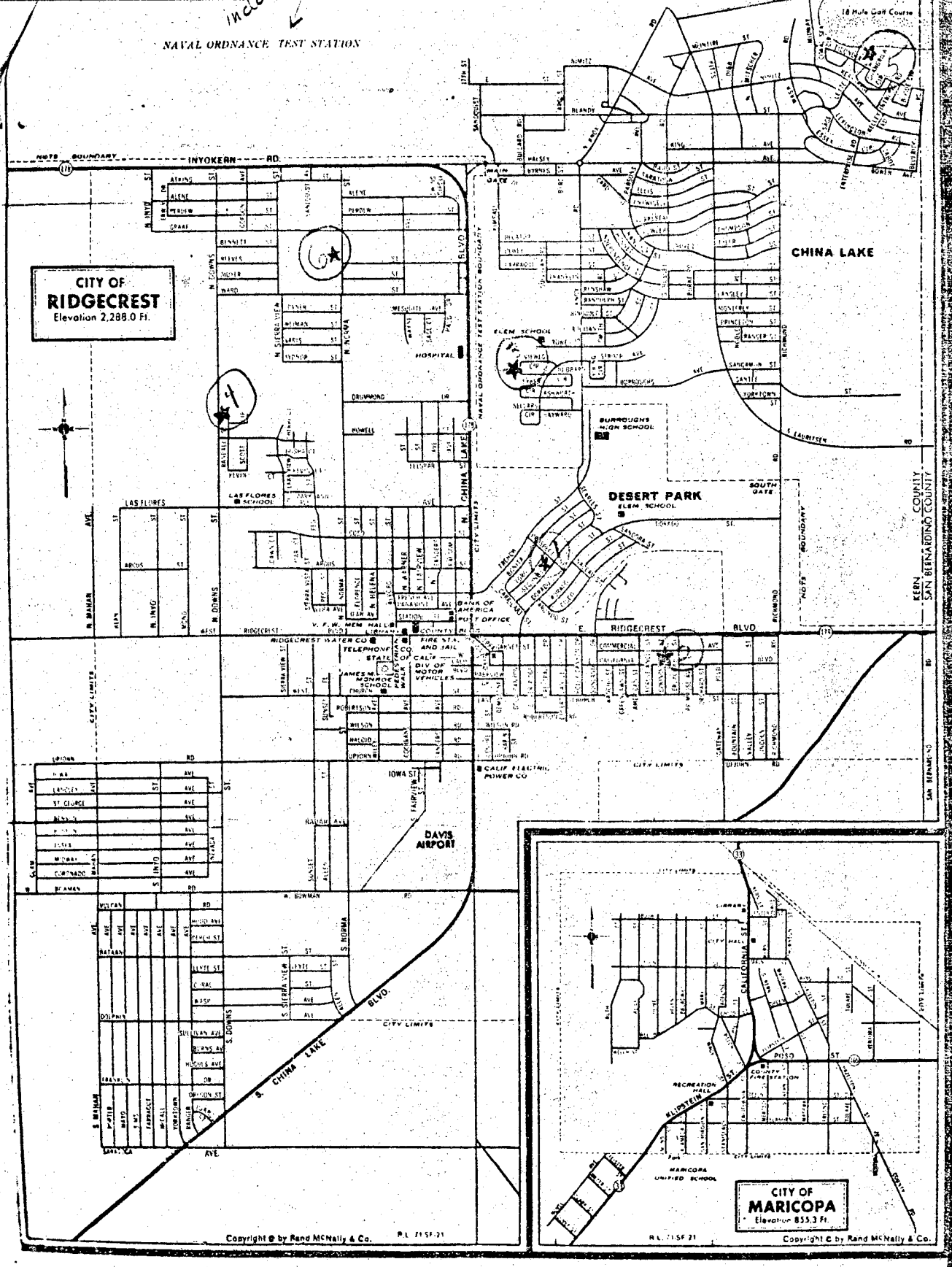

NAVAL ORDNANCE TEST STATION
INYOKERN RD.
CITY OF
RIDGECREST
Elevation 2,288.0 Ft.
CHINA LAKE
DESERT PARK
ELEM. SCHOOL
BURROUGHS HIGH SCHOOL
HOSPITAL
LAS FLORES SCHOOL
E. RIDGECREST BLVD
DAVIS AIRPORT
S. CHINA LAKE BLVD.
CITY LIMITS
KERN
SAN BERNARDINO COUNTY
CITY OF
MARICOPA
Elevation 855.3 Ft.
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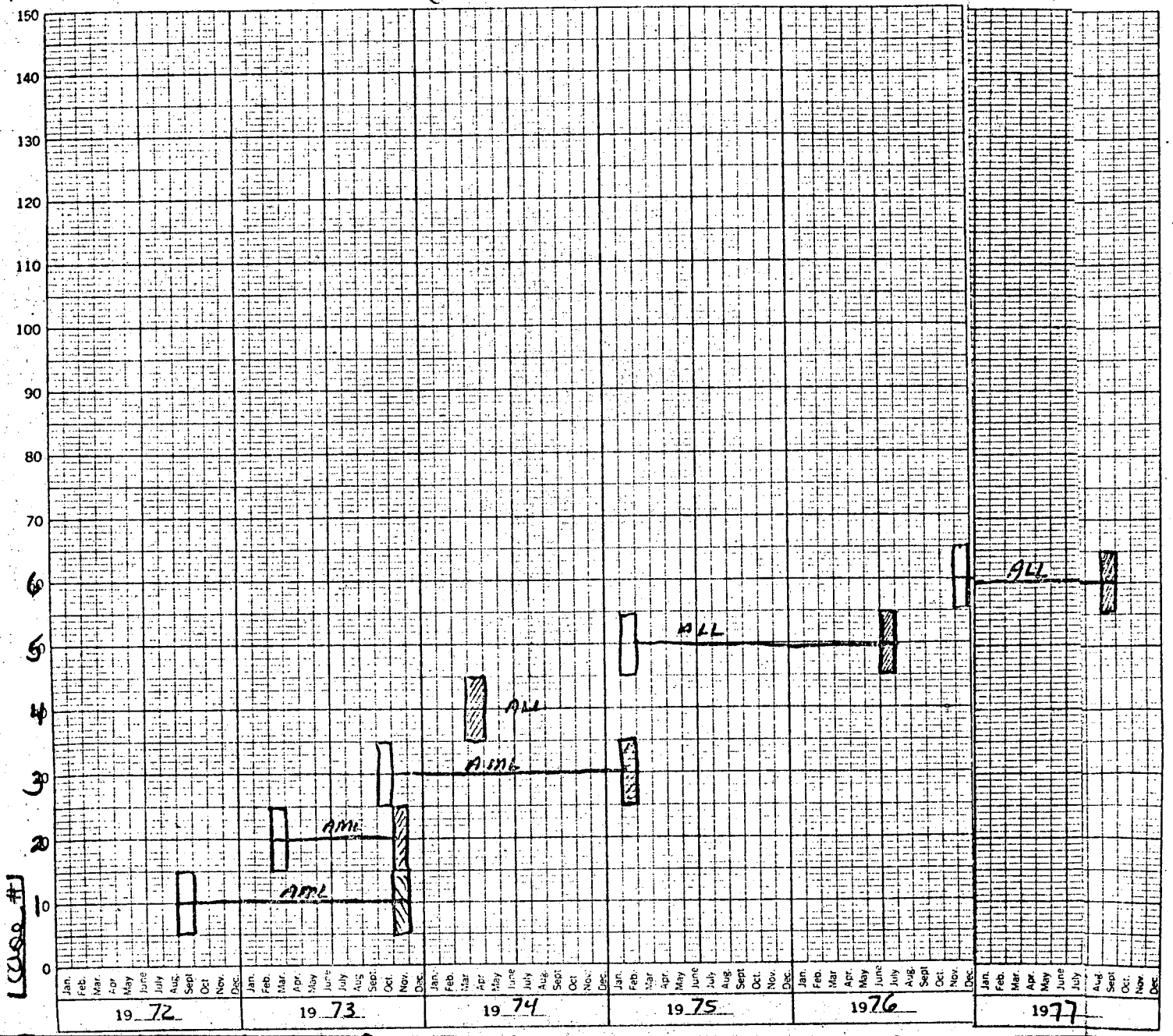
Fig One

Fig 2



150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Lease #1
AML
AML
AML
ALL
ALL
ALL
Jan. Feb. Mar. Apr. May June July Aug. Sept. Oct. Nov. Dec.
1972
1973
1974
1975
1976
1977