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Human

SURVEY MDL/2

PROSPECTIVE LONGITUDINAL EPIDEMIOLOGICAL SURVEY OF CLEAN-UP WORKERS AT WORK FROM 1980 IN HIGH-CONTAMINATED A ZONE

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REPORT ON SURVEY MDL/2

PROSPECTIVE LONGITUDINAL EPIDEMIOLOGICAL SURVEY OF CLEAN-UP WORKERS AT WORK FROM 1980 IN HIGH-CONTAMINATED A ZONE.

INTRCDUCTION

In A zone contaminated by high level of TCDD following the ICMESA accident the clean-up operations started in the summer of 1980. The existence of a real risk for clean-up workers is demonstrated by the experience accumulated in the last years as a result of similar operations at various European industrial plants in Europe.

Four years after the contamination episode at the Badische und Soda Fabrik (BASF) (two years after the reopening of the plant a new case of poisoning occurred in a worker who had been repairing an autoclave; during the operation he had several times lifted his protective mask to wipe off the sweat. Four days later dermatological manifestations and neurological symptoms appeared: six months later he was admitted to hospital for pancreatitis and hepatomegaly; nine months later he died; pancreatic necrosis, liver abscesses and chloracne on the trunk were found at necropsy

The clean-up procedures at the Coalite plant in England were inadequate: after the clean-up,79 cases of chloracne occurred in workers not exposed at the time of the accident.

Numerous cases of chloracne developed among workers engaged on the initial clean-up at the Philips plant in Holland. In the subsequent dismantling of the plant strict personal protection was enforced among the workers, who had to wear ventilated overalls, and a clinical surveillance program was set up centered on the evaluation of biochemical parameters before the event and subsequently at regu

lar intervals. No major deviations from normal values were observed in the ten workers who complied consistently with the prevention procedures. In two other workers who had been sent to the contaminated zone to dilute the contents of some tanks with water and who had worn on the overalls correctly one or more liver function parameters were found to be abnormal eleven weeks later; the values slowly normalised in the weeks that followed. In no case were there dermatological manifestations. The Philips researchers concluded that the working methods were effective in preventing exposure to TCDD.
Notwithstanding the vast quantity of data on TCDD that has accumulated since the Philips episode, a public health surveillance program still has to be based on the observation of biological parameters whose behavior may indirectly reveal exposure to the poison by showing its early effects (early effect indicators). Direct monitoring of the intake of the poison (dose indicator), up to now imply the biopsy of adipose tissue and it is not proposable as a continuous monitoring of groups of active workers in a plan of public health surveillance.

2 - METHODS

2.1 Objectives

The general objective of the survey was to gauge the efficiency of the safety measures taken during the clean-up of areas A1-A5. The safety measures were taken to prevent any significant exposure to the poison but, going by previous experience, possible exposure could not be excluded.

2.2 General design of the study

The design was that of a prospective controlled study (almost like a trial) comparing clean-up workers and reference groups. The parameters of interest (essentially clinical signs and symptoms, biochemical parameters) were measured before, during and after the period of potential exposure, in both groups (Fig. 1).

2.3 Population under study

The groups under study were selected at the preplacement examination. The subjects were sent by the firm handling the clean-up to Desio Hospital. None had previously been engaged on clean-up operations.

The preplacement examination took place in two stages: first 35 clean-up workers were selected and then a month later another 37 subjects were chosen, 36 as controls and 1 as a clean-up worker.

2.4 Preplacement examination. Data collection.

For every subject the preplacement examination included:

2.4.1 Interview-questionary

2.4.2 History and physical examination

2.4.3 Laboratory tests

2.4.4 Lung function test

2.4.5 Neurological examination, nerve conduction velocity and Electromyography (EMG)

2.4.6 Electrocardiogram (ECG)

2.4.7 Chest X-ray

2.4.1 Interview-questionary

The main purpose was to obtain informations for the comparision of the clean-up workers with the controls.

The interview-questionary was administered by two trained interviewers at the time of the medical examination. The questions included: universal variables (like years of schooling, marital status, telephone, working history), habit (drinking, smoking), drugs intake, family history and personal history with special reference to liver disease and skin diseases.

A copy of the questionary form is attached in Appendix A.

2.4.2 The history was taken and the physical examination done by occupational health specialists of the Occupational Health Service of Desio Hospital.

A copy of the case record form used is attached in Appendix B

2.4.3 Laboratory tests

The following tests were done:

1 - Glutamic oxalacetic transaminase (SGOT or AST)
2 - Glutamic pyruvic transaminase (SGPT or ALT)
3 - Alkaline phosphatase (AP)
4 - Gamma glutamyl transpeptidase (GGT)
5 - Bilirubin
6 - Cholesterol
7 - Triglycerides
8 - Surface antigen of hepatitis B Virus (HBsAg)
9 - Electrophoresis of serum proteins
10 - Blood cells count plus platelets and differential
11 - Total urinary porphyrins
12 - Urinary delta-aminolevulinic acid (ALA-U)

Most of the parameters were chosen because TCDD is hepatotoxic and affects the lipid metabolism. An increase in SGOT-SGPT is to be regarded as an indicator of cytolysis, an increase in GGT as an indicator of enzyme in

duction and an increase in AP as an indicator of biliary stasis.

The urinary porphyrins were determined because TCDD is known to exert a porphyrogenic effect.

2.4.4 Lung function test

2.4.5. Neurological examination, nerve conduction velocity, EMG

2.4.6 Electrocardiographic examination

2.4.7 Chest X-ray examination

2.5 Selection of groups of clean-up workers and controls

The criterium of eligibility was the fitness of the following parameters:

1 Males between 18 and 55 years old

2 No clinical signs of acute or chronic diseases such as viral hepatitis, diabetes, chronic liver disease, skin disease, etc.

3 Results within the normal range for the following laboratory tests: SGOT,SGPT,GGT,AP,Serum bilirubin,RBC,hematocrit,hemoglobin,WBC and differential counts,platelets,urinary porphyr

4 No clinical or instrumental signs of peripheral nervous sys

5 Normal ventilatory function test.

Out of 112 candidates only 72 were found eligible for the clean-up work and entered the study.

Grounds for exclusion were medical problems (liver disease, a normal values in laboratory tests), problems relating to the nature of the work (abnormalities of ventilatory function wit reduced tolerance to the wearing of a mask).

2.6 Periodic examinations

According to the protocol, every subject had to be examined every 6 months. Moreover, by regional law the clean-up worke had to be examined every 30 working days until the end of the

job. The periodic examinations included physical examination and laboratory test as required for the preplacement examination.

2.7 Final tests

The final tests were done 6 and 12 months after completion of the clean-up job.

2.8 Data analysis

Given the sample size the power of the tests used was estimated and proved to be adequate for the design of the study. The frequency distribution for the demographic and other variables (Table 1) was reported. For comparing this distribution the chi-squared test for independent samples was used. For the comparison of the continuous variates (Figs. 3-26) one- and two-way variance analysis was used, by group (clean-up and reference workers) and by test (tests done at successive examinations), using the SPSS program. All tests were rated significant if the probability depending on chance was less than 0.05% (with two tails).

Discriminant analysis was done with a program developed by Davies. The logic of the discriminant approach lies in the fact that significant differences could be identified for the entire battery of tests used, where for a single test no significant difference emerges.

RESULTS

The results of the preplacement examination and of the first 4 periodic examinations are reported here. The results will also be shown for the subset of individuals wich underwent all the periodic tests.

The data are also presented according to the number of hours worked. The time trend of six selected parameters for each worker is also indicated.

3.1 Response

The outline of the study design and follow-up response are shown in Fig. 1.

During the follow-up two of the exposed workers died in a road accident. One missed out after the first follow-up and yet another one after the second. Another four failed to attend for the fourth follow-up.

In the reference group the response rate was low: five failed to attend for the first follow-up, seven for the second and third and another six for the last (response rate = 65%).

Among the clean-up workers the response rate was 100% of those present on the job, who needed to comply with periodical control and to be passed fit to continue working.

The fall in the response rate at the last follow-up was due to ex clean-up workers (those who had for various reasons given up working in the zone). In the reference group the low response rate was due to distance from the place of residence or to emigration to other areas. One control subject after the first follow-up was included among the clean-up workers and from that date he was excluded from the data analysis

3.2 Base data

3.2.1 Interview-questionary

One of the clean-up workers and four of the controls were not interviewed. Inter-group comparability in respect of certain characteristics is indicated in Table 1. Age, education, marital status, smoking, drinking, previous exposure to hepatotoxic substances and history of skin dis-

ease presented fairly similar distributions in the two groups. Significant differences were found in respect of history of liver disease and possession of a telephone at home, which proved to be more frequent in the reference group.

3.2.2 Laboratory data

Of the laboratory tests done those most relevant for statistical analysis are the ones that, according to the scientific literature, seem to be correlated with exposure to TCDD, viz. urinary porphyrins, liver enzymes, serum cholesterol and triglycerides. The results of the WBC, platelet, serum protein, albumin and gamma globulin tests are also presented. At the preplacement examination no significant difference was found in the variables studied, except for alkaline phosphatase, the mean value of which was higher in the reference group.

3.3 Follow-up results

During the follow-up period nine workers left the job for reasons unrelated to health. Five workers were rated no longer fit and were dismissed. The grounds for unfitness were:

1 - in subject 12 abnormal SGOT (42 mU/ml) and SGOT (75 mU/ml) values in two tests, in October and December 1981; these values returned to normal in subsequent tests.
2 - in subject 13 severe hypertension (195-125 mmHg).
3 - in subject 14 a slight increase in GGT.
4 - in subject 16 persistent presence of HBsAg.
5 - in subject 27 use of antiepileptic drugs.

These subjects continued to attend for follow-up examinations according to the program for ex clean-up workers. Another subject gave up the job a few days after starting because he could

not stand the mask and was lost to follow-up.

3.3.2 Clinical evaluation

No case of skin or neurological disease occurred. Clinical examination revealed nothing noteworthy. The percentage of subjects with hepatomegaly did not differ significantly in the two groups; the higher percentage among the clean-up workers might be due to the fact that the doctors were not "blind" (Fig. 2). No significant difference emerged in respect of weight variations.

3.3.3 Laboratory data

The analysis was done separately for all the cases in the follow-up period and for a subset of subjects whose data were available for all the periodic examinations (except the last).

Dispersion charts for 10 out of 14 laboratory tests in the first four examinations are shown in Figs. 3-26 together with the means and standard deviations.

3.3.3.1 Urinary porphyrins (Figs. 3 and 4)

No significant difference was found between the t groups at successive tests but a significant diff ence was found for both groups between tests done successive times. But the values were within nor limits, well below threshold values. The same re sults appeared for the subset of subjects always present.

3.3.3.2 SGOT - SGPT (Figs. 5,6,7,8)

No significant difference was found, except for S at third follow-up, when the mean value of the ex posed (17.75 mU/ml) was higher than in the non ex posed (14.28); this difference was also significa within the subgroup of ever-present subjects.

3.3.3.3 Alkaline phosphatase (Figs. 9-10)

The significant difference observed in the baseline test disappeared in subsequent tests.

3.3.3.4 Gamma GT (Figs. 11-12)

No significant difference was found between the two groups in the successive tests but a significant difference did emerge for both groups between successive tests.

3.3.3.5 Bilirubin (Figs. 13-14)

Serum total bilirubin behaved in the same way as GGT.

3.3.3.6 ALA-U (Figs. 15-16)

The same applies to ALA-U.

3.3.3.7 Cholesterol and triglycerides (Figs.17-18-19-20)

No difference was observed.

3.3.3.8 Other laboratory tests

A significantly lower WBC count was found in the clean-up workers at first follow-up (Figs. 21 and 22) and the same applies to platelets (Fig. 23). The serum total protein value was higher than in the controls (Fig. 24) and a lower mean serum albumin (Fig. 25) in the clean-up workers in the preplacement examination only in the subgroup of the ever-present. A significantly higher gamma globulin value (Fig.26) was found in the clean-up workers at second follow-up.

3.3.3.9 Analysis of the binary data

In order to identify deviations from the normal values, some variables were converted into binary data, above or below the threshold used at the preplacement examination. The frequency of outside range values was too low for statistical analysis: no noteworthy difference in the percentages of abnormal values was

3.3.3.10 Discriminant analysis

The dispersion chart of the scores obtained by discriminant analysis of the values of eleven laboratory tests is shown in Fig. 37. No significant discriminant function was identified.

3.4 On-job hours and laboratory tests

The clean-up workers were divided into three subgroups by the number of hours worked in zone A at the time of the second follow-up. Seven had worked less than 200 h, nine from 201 to 400 h and twenty more than 400 h. No significant difference in the mean values of the lab tests was found at the first and second follow-up (Table 2).

3.5 Individual assessment of the clean-up workers

It must be stressed that, while the program of tests for the reference group envisaged an examination every six months, the clean-up workers underwent medical checks every 30 days as long they continued on the job. The number of examinations of this group was between 2 and 20 (mean 12.41). In the foregoing analysis we have considered only the five for which the control data are also available. Figs. 38 to 73 show the time trends of six selected parameters (porphyrins, SGOT, AP, GGT, cholesterol and triglycerides) for each worker.

The analysis of the test shows that in ten cases (nos. 4,10,16, 20,22,23,27,31,32 and 35) no variables increased by more than 100% of the baseline value during the follow-up period; in thirteen cases (nos. 1,2,3,5,6,14,15,18,19,25,29,30 and 33) there was an increase of more than 100% in at least one parameter but always within the normal range. In another thirteen cases (nos. 3,9,11,12,13,17,21,24,26,28,34,36) there was an increase of more than 100% in at least one parameter with values beyond the nor

range: in six cases the increase was in the triglycerides, in three in alkaline phosphatase, in one the urinary porphyrins and triglycerides, in one case transaminase and triglycerides and in one case GGT.

CONCLUSIONS

The program of surveillance for the clean-up workers in area A1-A5 of Seveso was undertaken to check the efficiency of the safety measures taken during the clean-up operation started in May 1980. The principal conclusions are:

1. During the follow-up period no case of clear clinical disease that could be attributed to TCDD (chloracne, peripheral neuropathy, liver disease, etc.) occurred.

2. Of the five workers rated unfit after the commencement of the job one had abnormal liver enzyme values in two tests, which subsequently normalised. There was no known cause of the increase and so a transient effect of TCDD exposure cannot be excluded, although the contemporaneous weight gain (more than 15 kg) may suggest nutritional causes.

3. No definite difference between clean-up workers and controls was found in respect of the laboratory tests. The same conclusion was reached when the data were treated as binary data and discriminant analysis was applied to 13 lab test variables.

4. The analysis of the time trends of six variables in the clean-up workers shows that some variations occurred in the triglycerides: these are, however, more likely to be due to biological variability or to insufficient precision in analysis.

In sum, the survey failed to show biologically significant features

such as to suggest that the workers engaged on the clean-up operations in the highly contaminated zones can have absorbed TCDD. The safety measures adopted seem to have provided effective protection for the workers.

Desio, 30 July 1983.

TABLE 1. Distribution of Demographic and Other Variables in Clean-up and Reference Groups

Characteristics	Clean-up Workers	Reference Workers
Mean Age	31.2	32.7
	t=.74	
Education (Years completed)		
0-5	13	19
6-9	15	10
10+	7	3
	Chi sq_{2df}=3.59	
Marital Status		
Never Married	13	19
Married	15	10
Separated,Divorced Widowed	2	0
	Chi sq_{2df}=3.54	
Smoking Habit (Cigarettes/day)		
Non-smoker	11	8
Ex-smoker	2	5
Less than 20	11	7
20 or more	11	12
	Chi sq_{3df}=2.56	
Alcohol Consumption (cc./day)		
0	7	6
Less than 40	9	12
40 or more	19	14
	Chi sq_{2df}=1.13	
Previous Exposure to Hepatotoxic Substances		
Yes	3	7
No	32	25
Chi sq_{1df}=2.33		

TABLE 1. Distribution of Demographic and Other Variables (Continued) in Clean-up and Reference Groups

Characteristics	Clean-up Workers	Reference Workers
Telephone at Home		
Yes	13	21
No	22	11
	Chi_{1df} sq.=5.43*	
History of Dermatitis		
Yes	6	9
No	29	23
	Chi sq_{1df}=1.16	
History of Liver Enlargement		
Yes	4	12
No	29	23
	Chi sq_{1df}=6.25*	
Past Physician's Warning on Liver Disease		
Yes	4	4
No	32	28
	Chi sq_{1df}=.03	

*Significant at p less than .05

TABLE .2 Results of various laboratory tests (mean and *standard deviation*) at the pre-employment examination, after 3 and 9 months in the decontamination workers, divided according to the number of hours spent in A1, A2 zones.

Number of hours	less than 200			from 201 to 400			more than 400		
	pre-empl.ex.	3rd month ex.	9th month ex.	pre-empl.ex.	3rd month ex.	9th month ex.	pre-empl.ex.	3rd month ex.	9th month
Total urinary porphyrine (µg/g.creat.)	71.17 *(24.10)*	89.20 *(47.20)*	60.43 *(16.67)*	93.67 *(54.55)*	75.89 *(31.54)*	81.00 *(21.05)*	96.44 *(44.29)*	70.55 *(38.64)*	66.96 *(27.*
SGOT (U/L)	20.71 *(4.11)*	10.83 *(6.05)*	10.29 *(4.89)*	15.56 *(2,70)*	14.67 *(2.12)*	12.67 *(3.24)*	15.20 *(3.02)*	14.75 *(4.58)*	13.50 *(3.6*
SGPT (U/L)	23.71 *(6.32)*	20.33 *(3.67)*	19.14 *(6.72)*	16.78 *(5.83)*	14.89 *(3.10)*	12.00 *(2.96)*	17.70 *(4.07)*	19.35 *(8.05)*	16.80 *(6.2*
Alkaline phosfatase(U/L)	23.86 *(5.93)*	34.03 *(8.18)*	27,71 *(5.02)*	34.67 *(11.88)*	37.11 *(6.45)*	33.56 *(7.04)*	27.20 *(6.71)*	32.15 *(7.51)*	20.70 *(7.*
Gamma-GT (U/L)	30.00 *(10.07)*	31.67 *(12.14)*	26.29 *(10.87)*	18.78 *(12,36)*	23.11 *(12.06)*	20.56 *(7.62)*	17.95 *(8.01)*	20.85 *(7.20)*	18.05 *(7.*
Total Billirubin(mg/dl)	.73 *(.13)*	.58 *(.16)*	.67 *(.18)*	.66 *(.16)*	.62 *(.17)*	.59 *(.15)*	.66 *(.13)*	.65 *(.12)*	.57 *(.1*
PTI (sec)	27.25 *(2.43)*	27.58 *(3.22)*	29.67 *(3.27)*	27.06 *(1.71)*	26.29 *(2.21)*	29.59 *(2.57)*	25.55 *(2.33)*	26.60 *(2.80)*	28.71 *(1.*
Hemoglobin (g/dl)	15.80 *(.60)*	15.93 *(.74)*	16.31 *(.66)*	16.06 *(.90)*	16.01 *(.82)*	16.51 *(.91)*	15.64 *(.73)*	15.65 *(.76)*	16.16 *(.9*
WBC ($x10^3/mm^3$)	6.46 *(1.69)*	7.15 *(2.96)*	6.06 *(1.85)*	6.73 *(1.30)*	6.67 *(2.25)*	6.81 *(1.72)*	6.89 *(1.19)*	6.91 *(1.50)*	6.16 *(1.*
Platelets ($x10^3/mm^3$)	216.14 *(47.34)*	230.17 *(43.86)*	222.00 *(40.85)*	200.89 *(42.51)*	209.56 *(44.51)*	208.78 *(36.77)*	193.25 *(34.68)*	205.20 *(67.36)*	196.20 *(38*
Albumin(g/dl)	4.80 *(.22)*	4.97 *(.45)*	4.98 *(.36)*	4.62 *(.33)*	4.96 *(.44)*	4.29 *(.18)*	4.70 *(.33)*	4.78 *(.36)*	5.05 *(.1*
Gamma-Globulins (g/dl)	1.02 *(.13)*	.96 *(.13)*	.94 *(.11)*	1.22 *(.17)*	1.17 *(.22)*	1.15 *(.12)*	1.21 *(.20)*	1.18 *(.20)*	1.16 *(.1*
Cholesterol Serum Level (mg/dl)	242.43 *(60.38)*	223.50 *(57.68)*	215.71 *(63.50)*	184.78 *(33,24)*	192.78 *(30.89)*	192.89 *(26.56)*	174.11 *(25.22)*	179.60 *(23.61)*	183.80 *(2*
Triglycerides (mg/dl)	148.43	155.17	131.00	112.56	109.56	136.56	101.37	96.3	134.30
			(24.16)	*(38.85)*	*(46.59)*	*(43.42)*	*(42.36)*	*(86.29)*	*(5*

FIG. 1 OUTLINE OF THE STUDY DESIGN AND FOLLOW-UP RESPONSE AMONG CLEAN-UP AND REFERENCE GROUPS

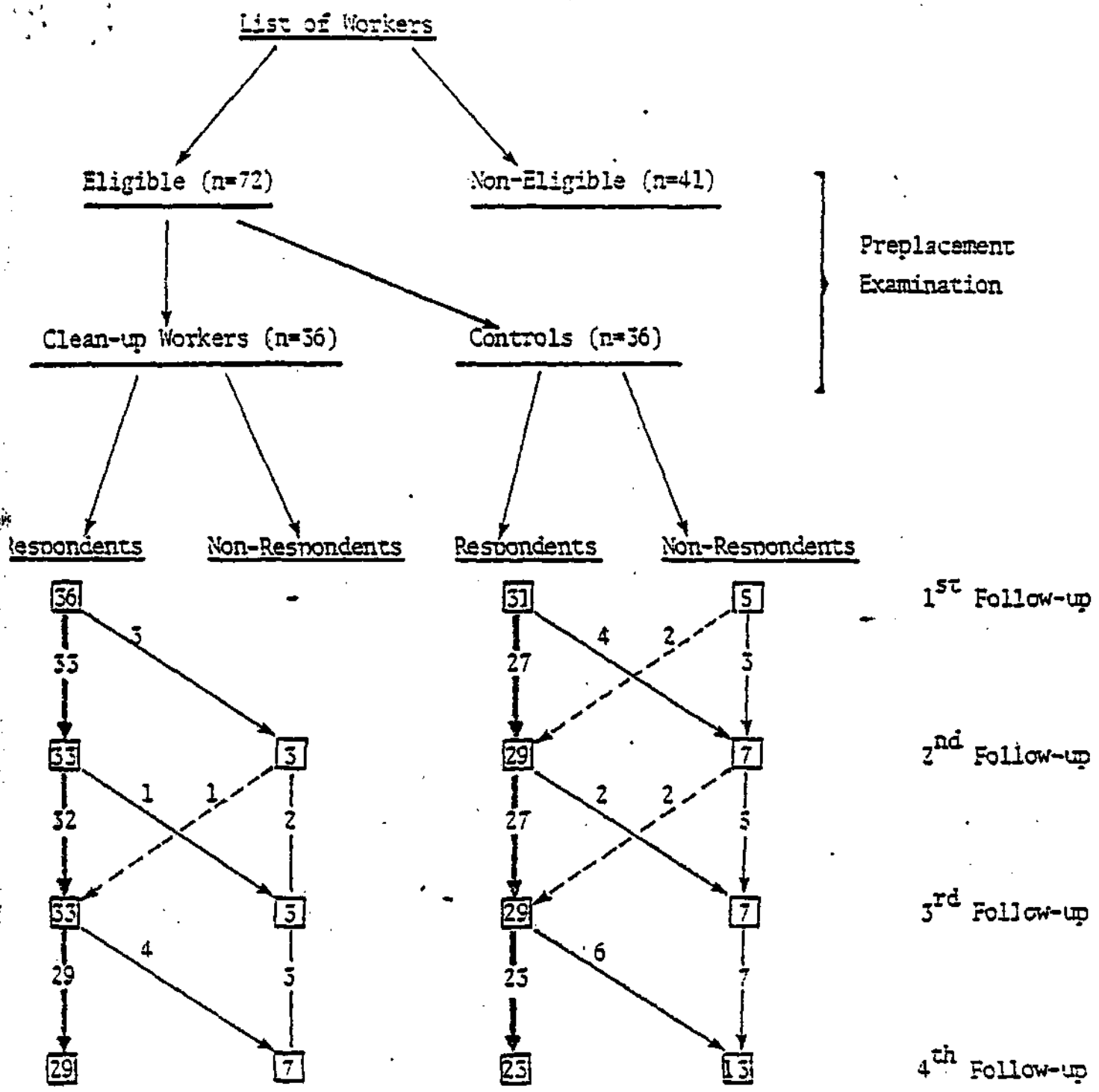


FIG.2 PROPORTION OF LIVER ENLARGEMENT AMONG CLEAN-UP AND CONTROLS.

CLEAN-UP WORKERS ——

CONTROLS .....

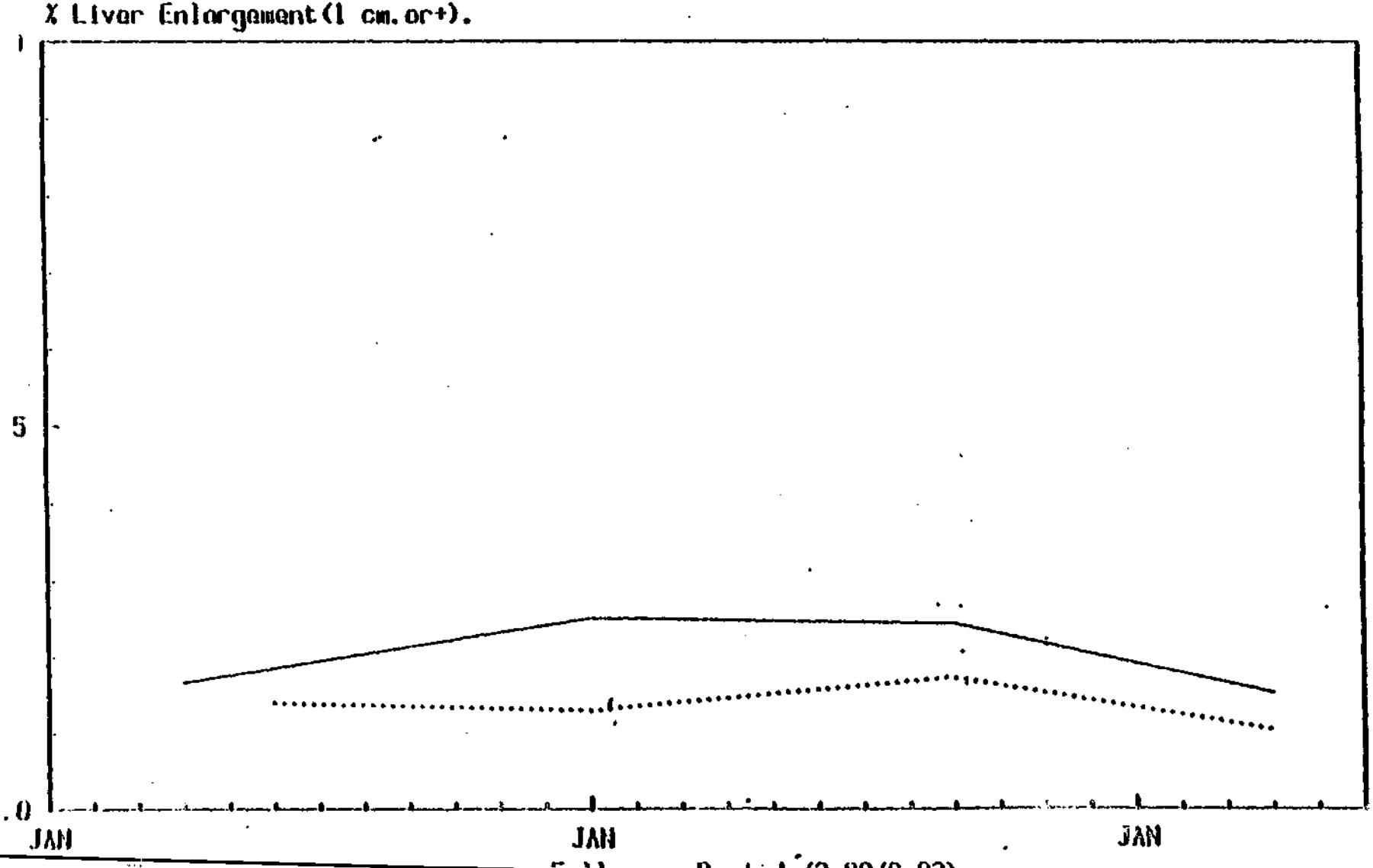


Fig. 3 URINARY PORPHYRINS VALUES
in clean-up and reference groups

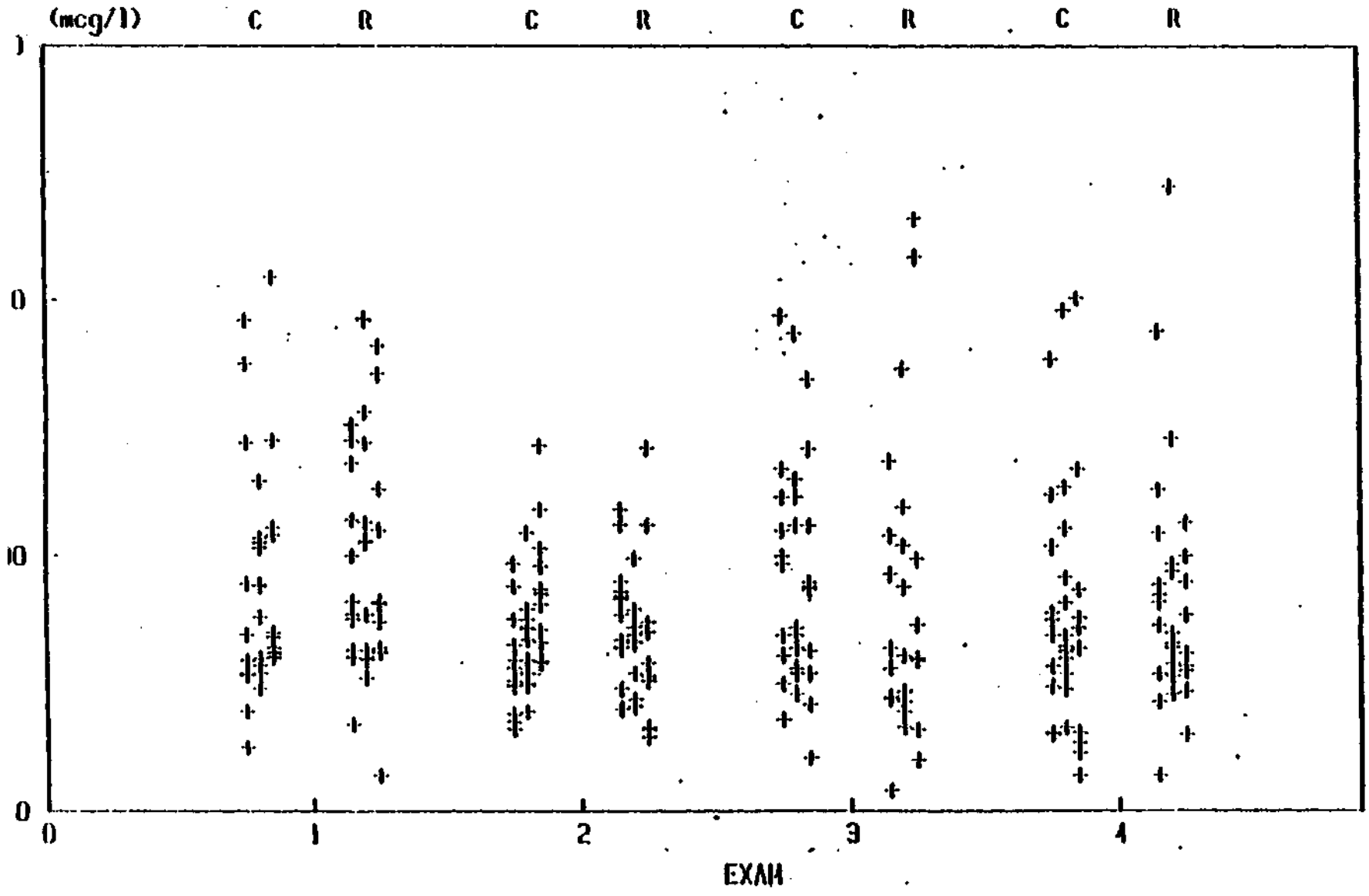
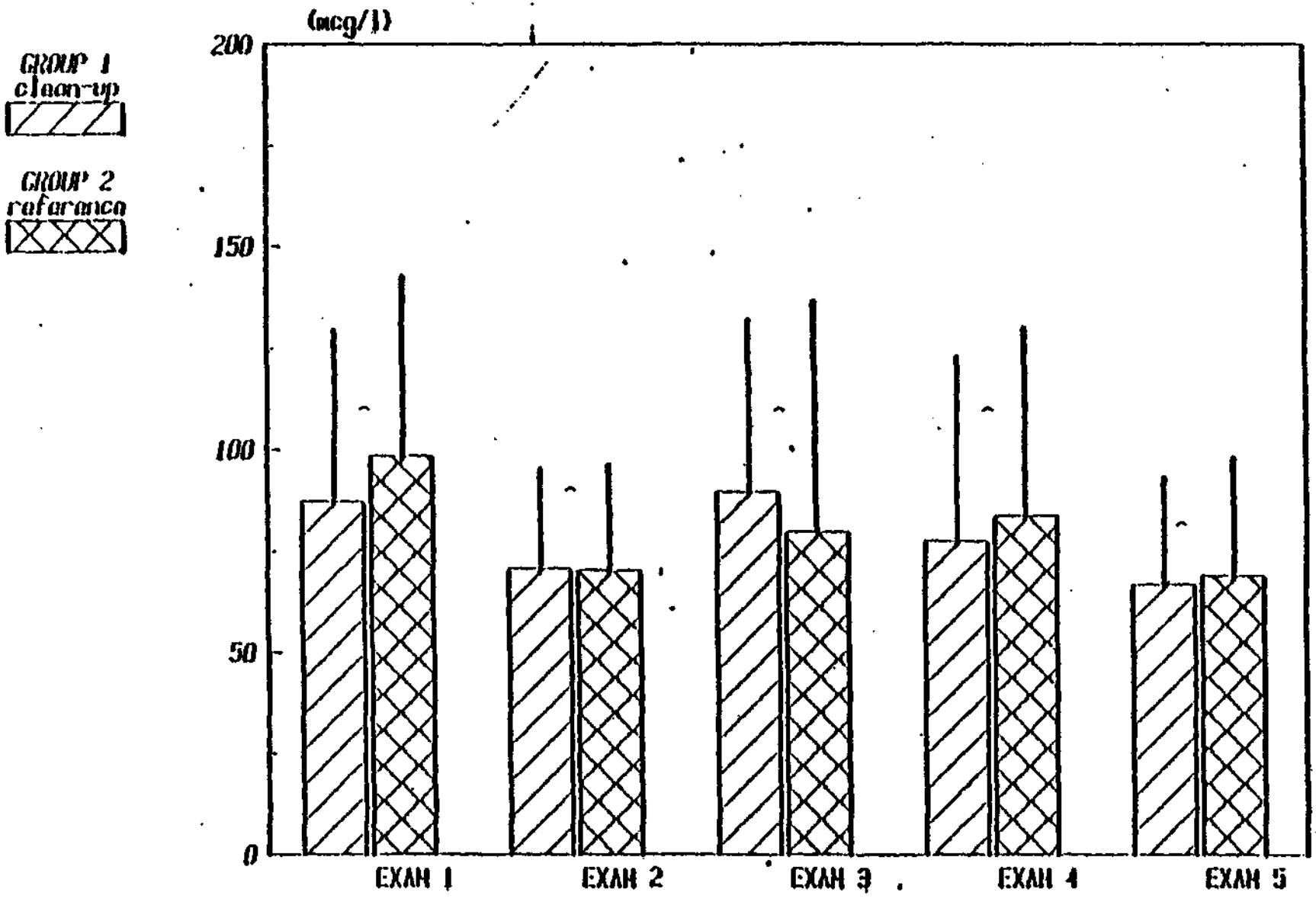


Fig.4 URINARY PORPHYRINS (mean+sd)

in clean-up and reference groups



* Significant between-exams mean difference.

Fig.5 S G O I values
in clean-up and reference groups

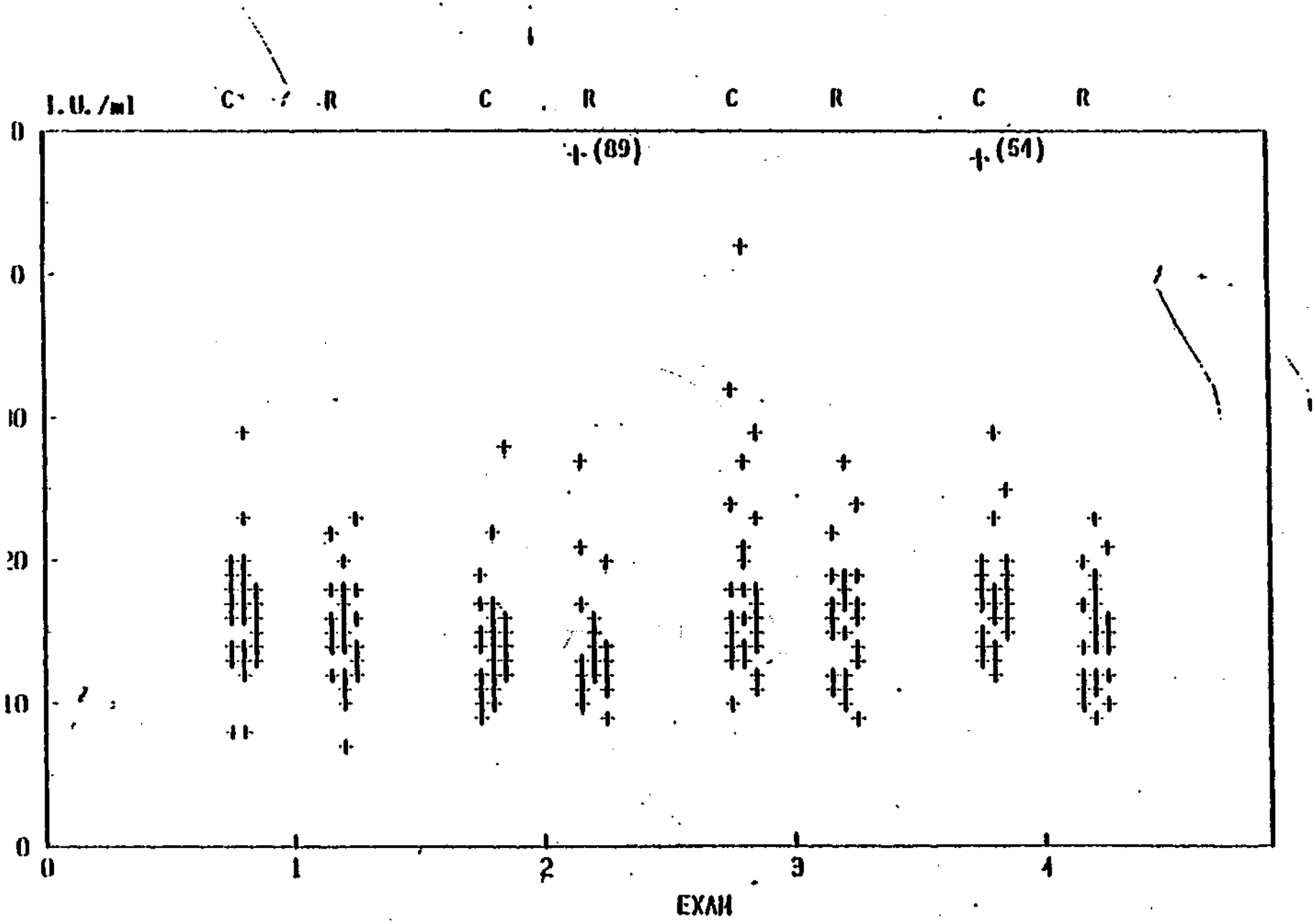
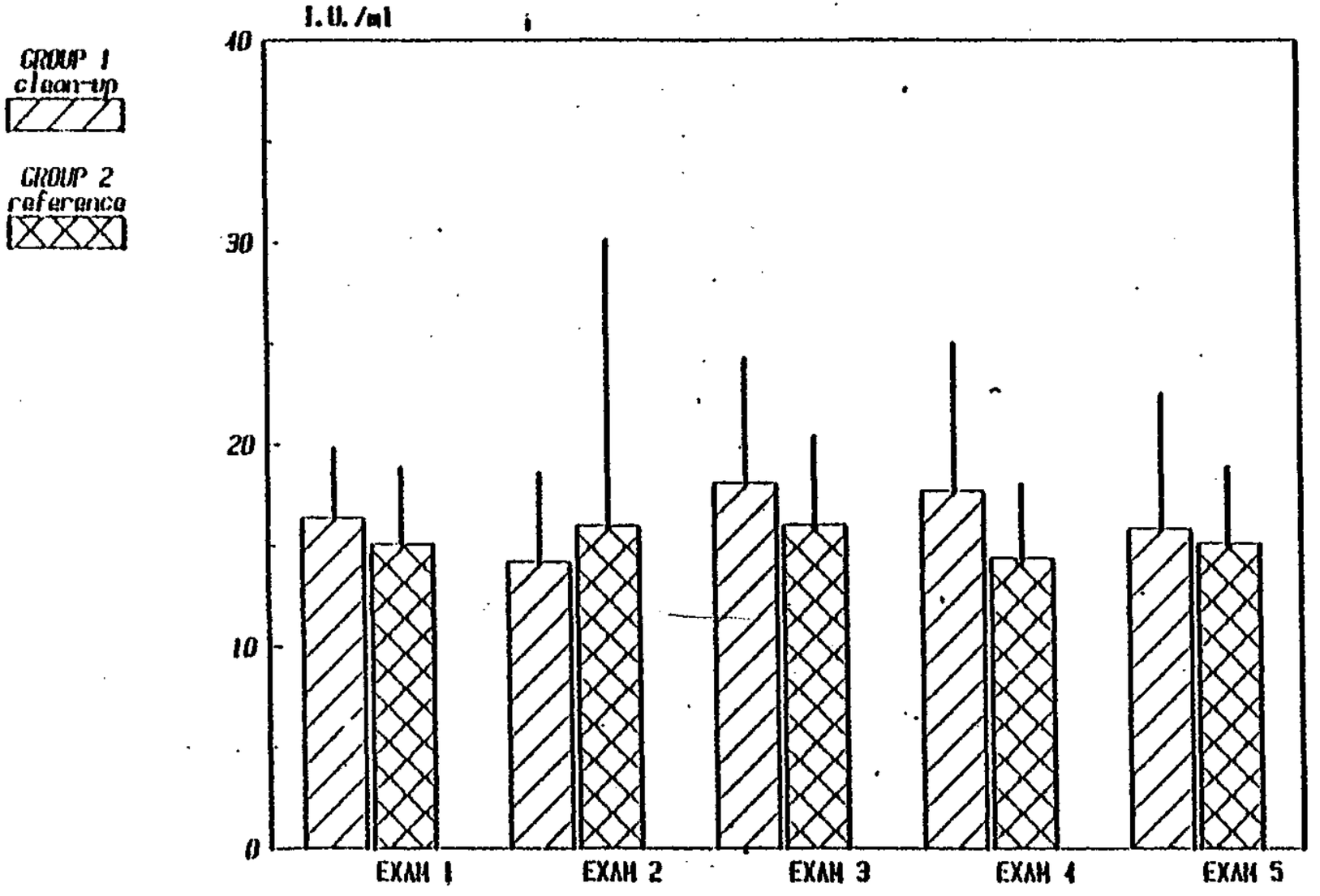


Fig. 6 S. G. O. T. (mean+sd)

in clean-up and reference groups



^ Significant between-groups mean difference.

Fig.7 S G P T values
in clean-up and reference groups

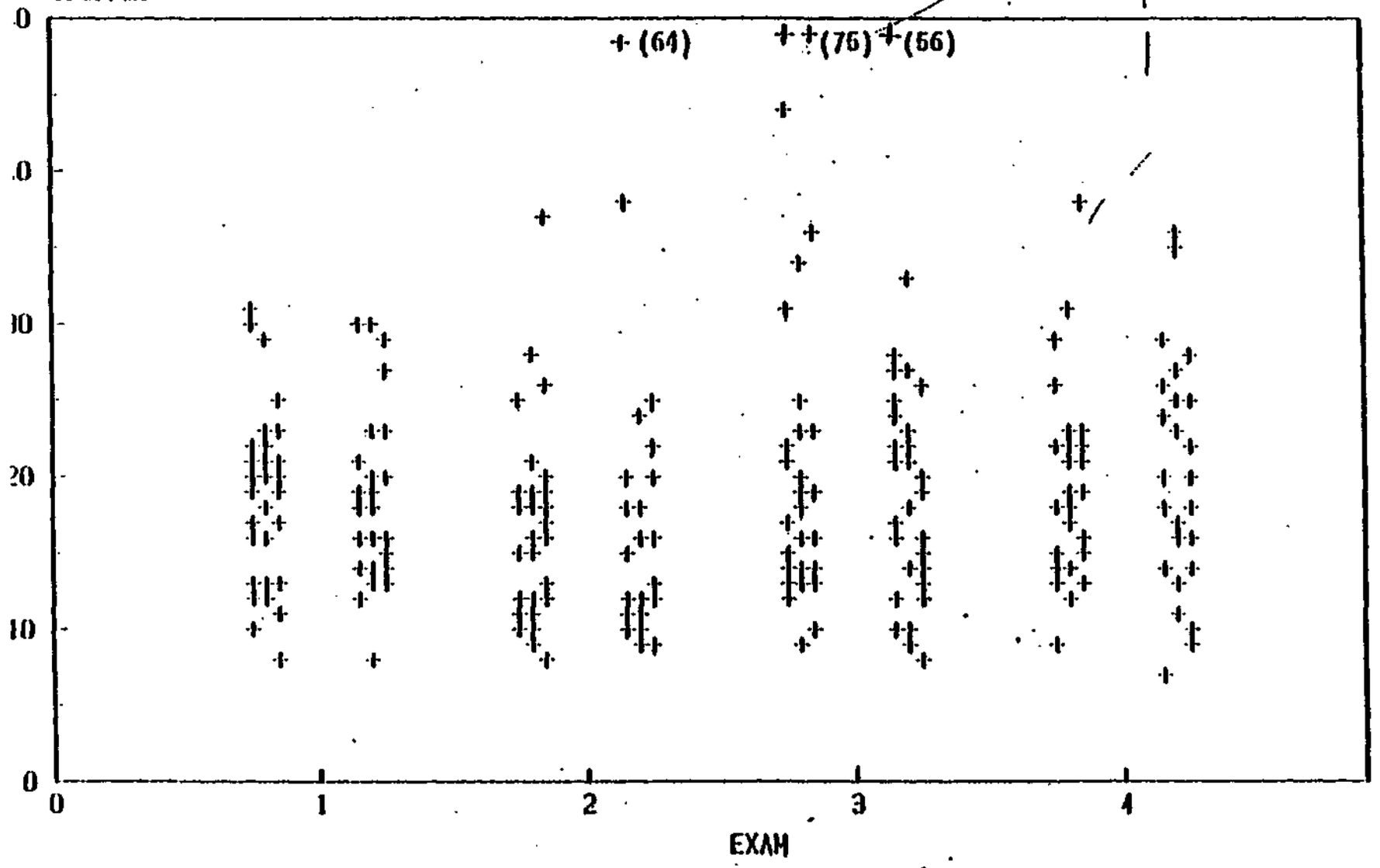


Fig.9 ALKAL. PHOSPHATASE value
in clean-up and reference groups

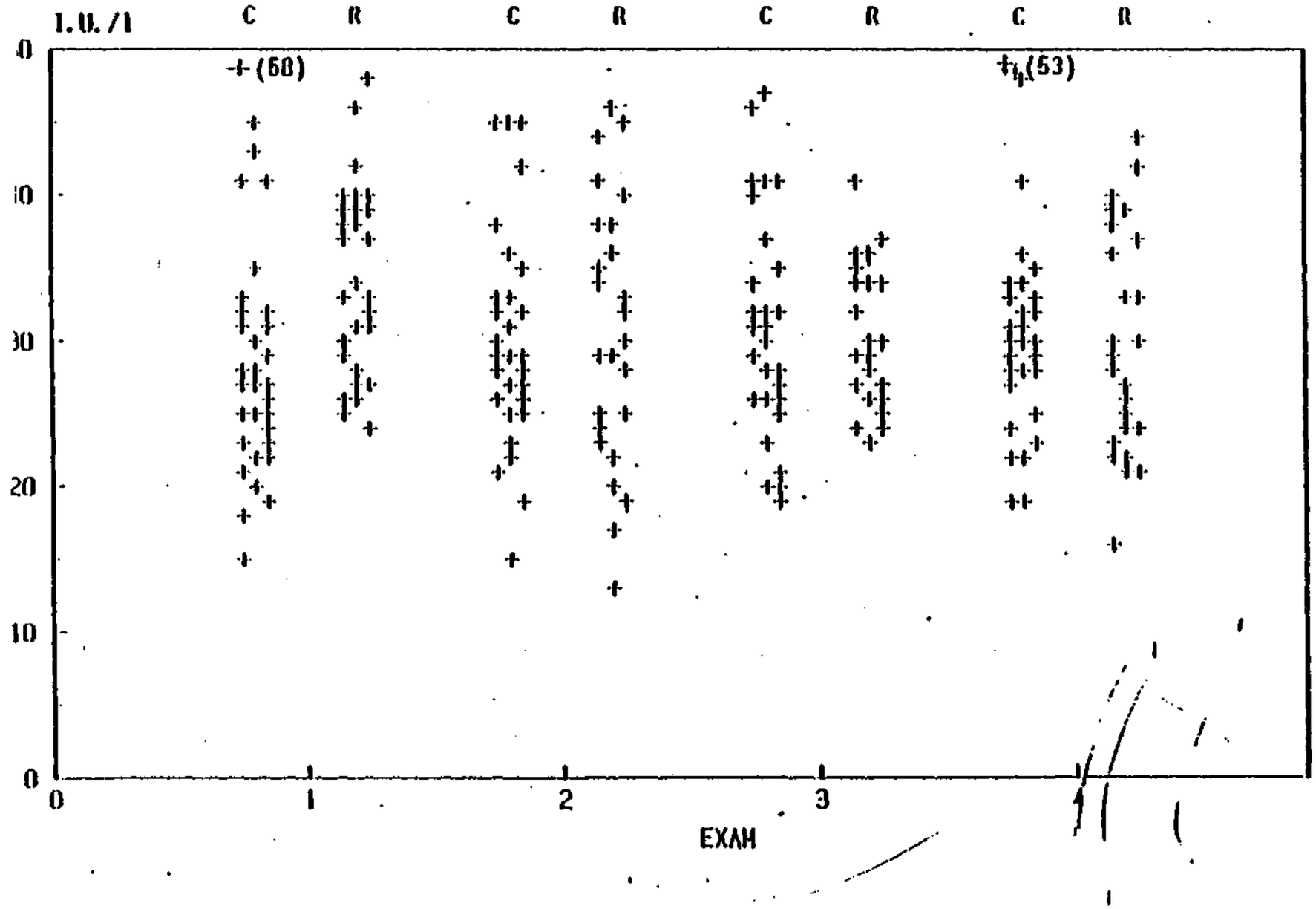


Fig.8 S.G.P.T. (mean+sd)

in clean-up and reference groups

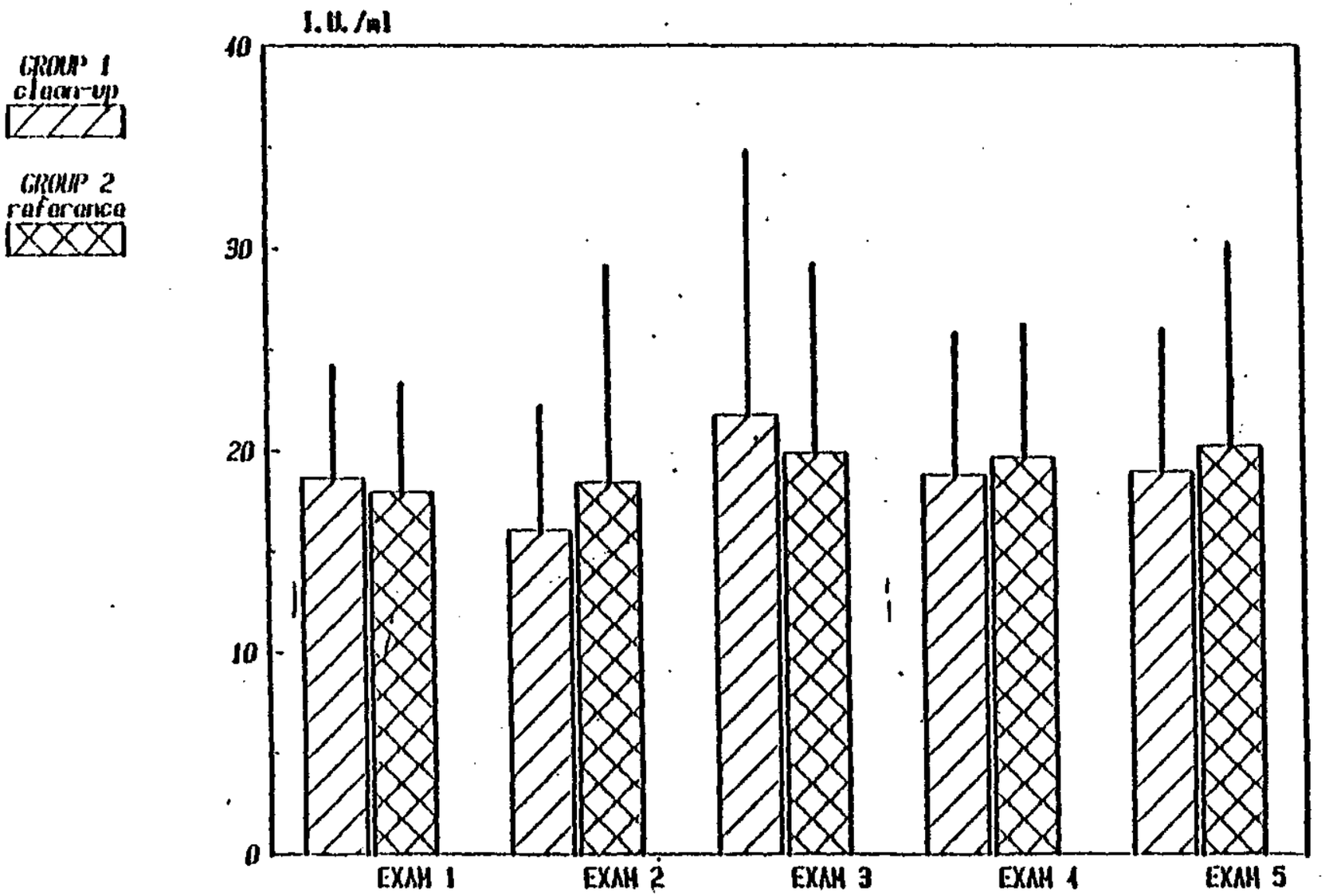
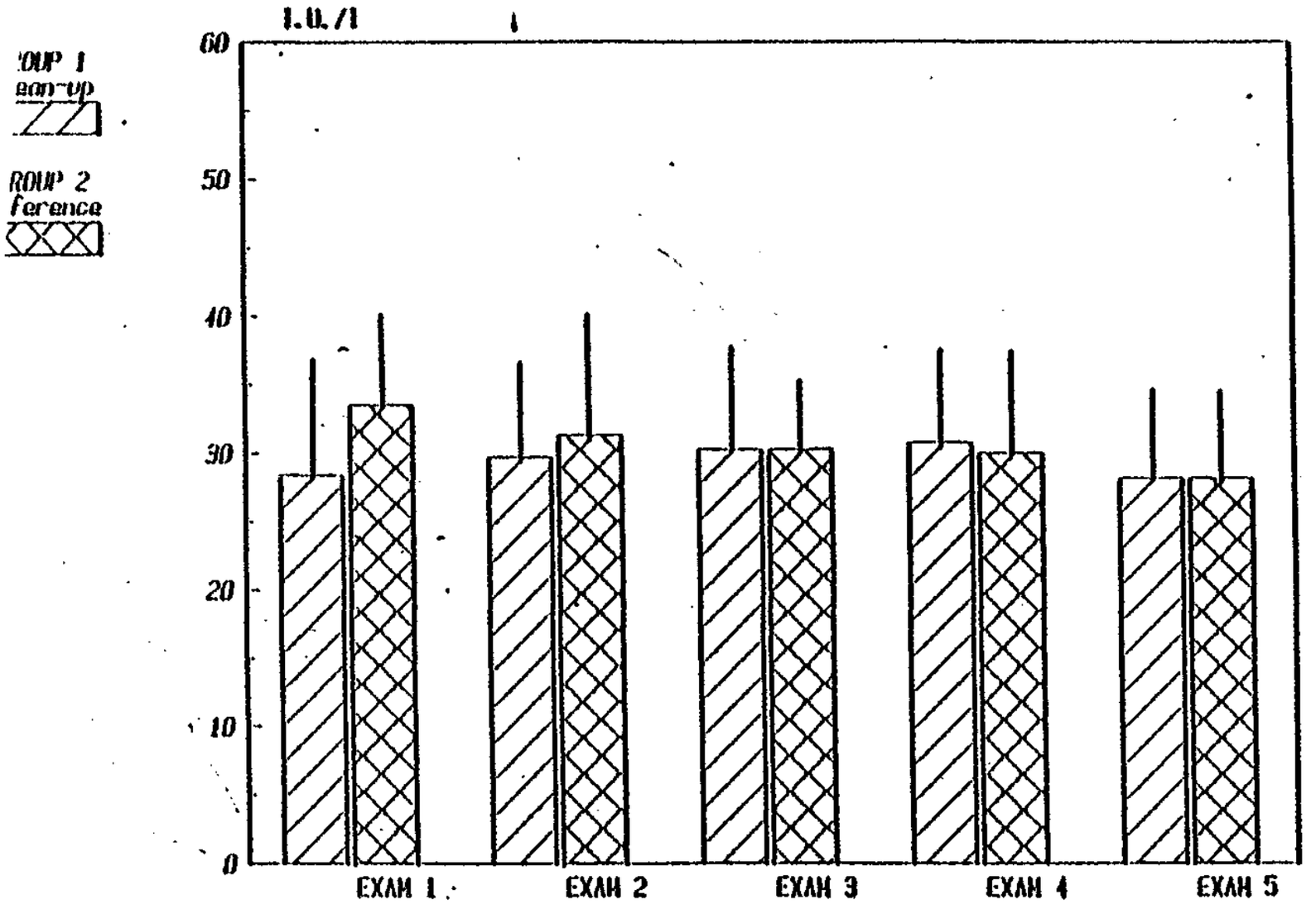


Fig.10ALKAL. PHOSPHATASE (mean+sd)
in clean-up and reference groups



* Significant between-groups mean difference.

Fig.11 G G T P values
in clean-up and reference groups

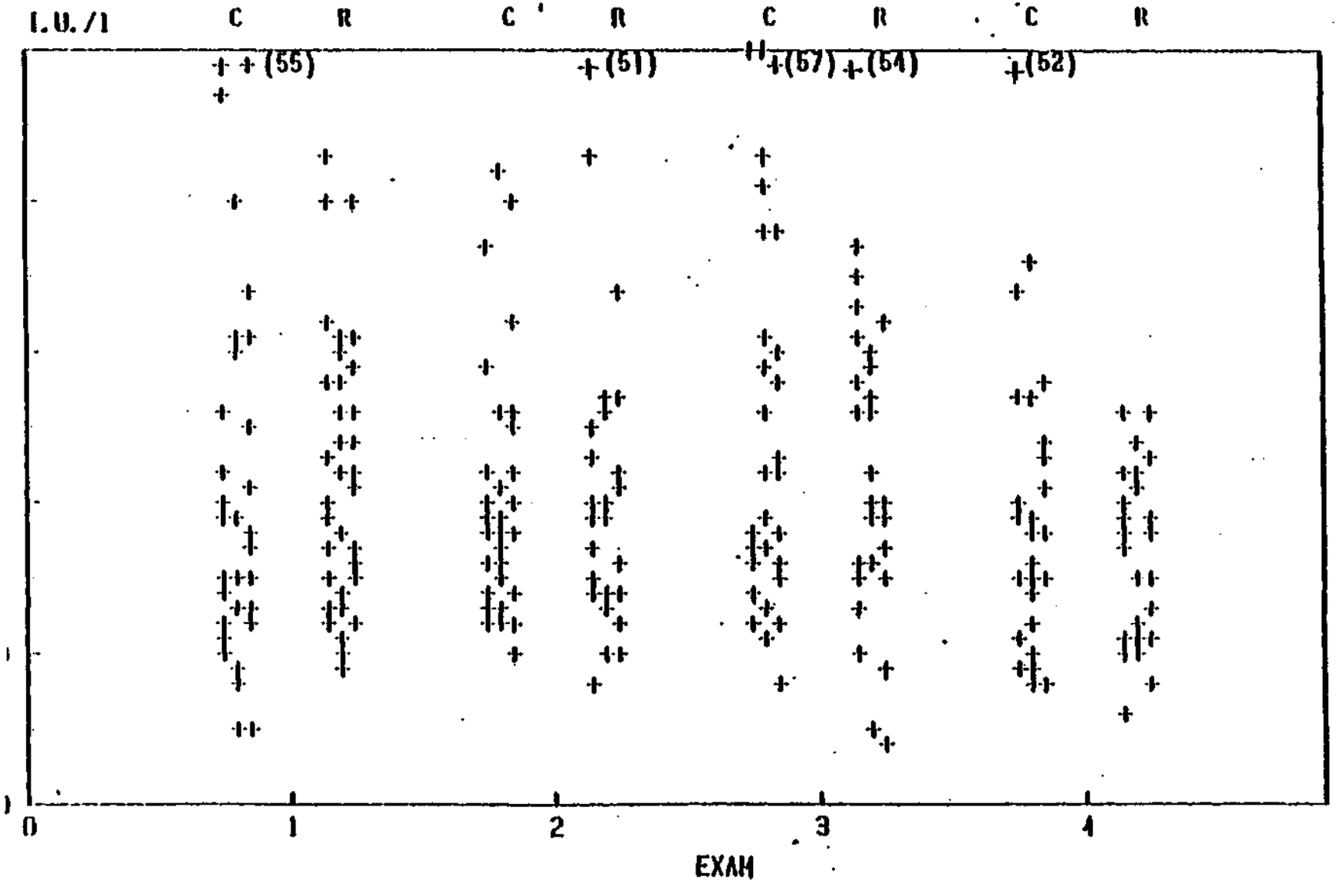
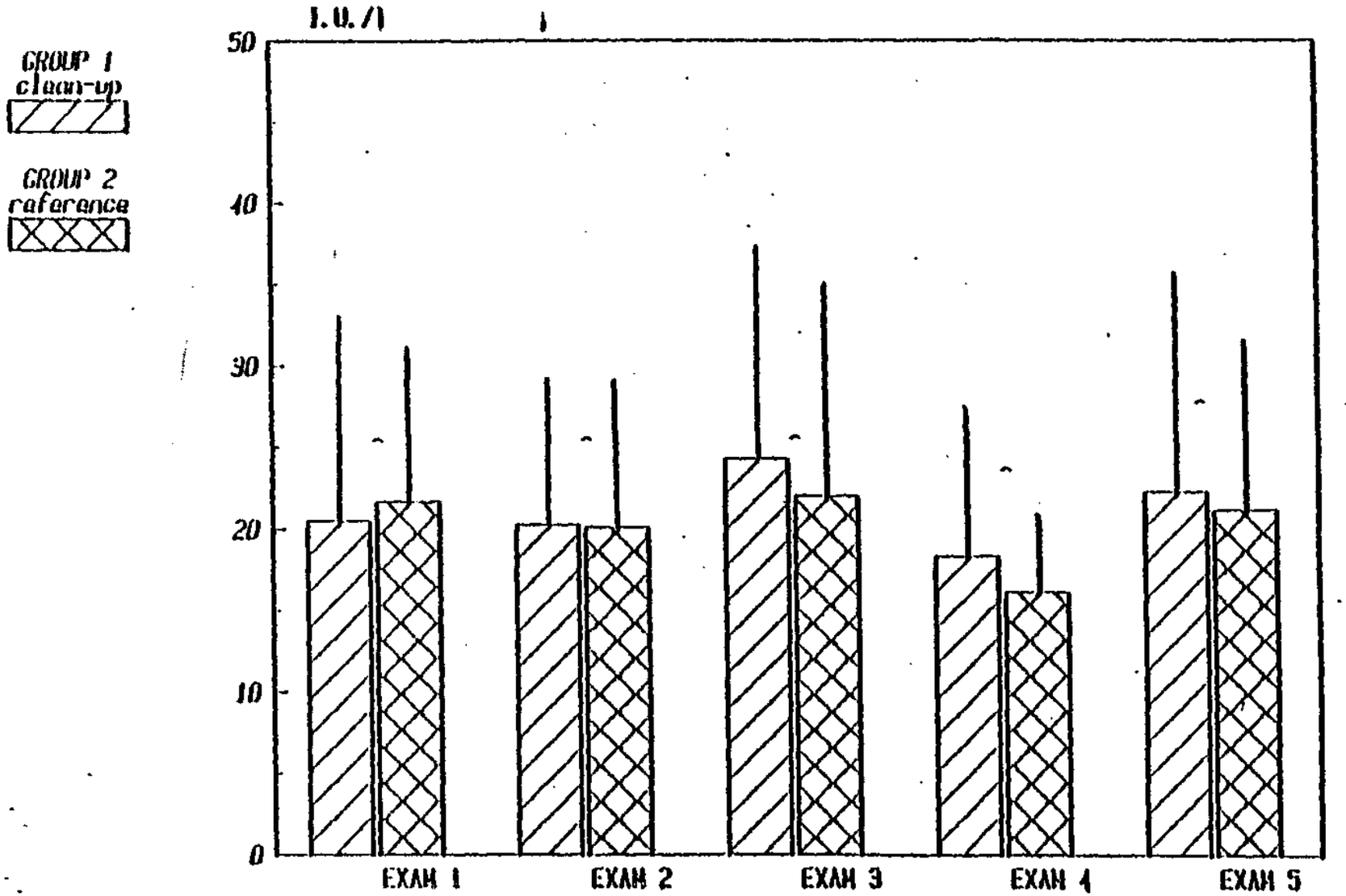


Fig. 12 G. G. T. P. (mean+sd)
in clean-up and reference groups



^ Significant between-exams mean difference.

Fig. 13 BILIRUBIN values
in clean-up and reference groups

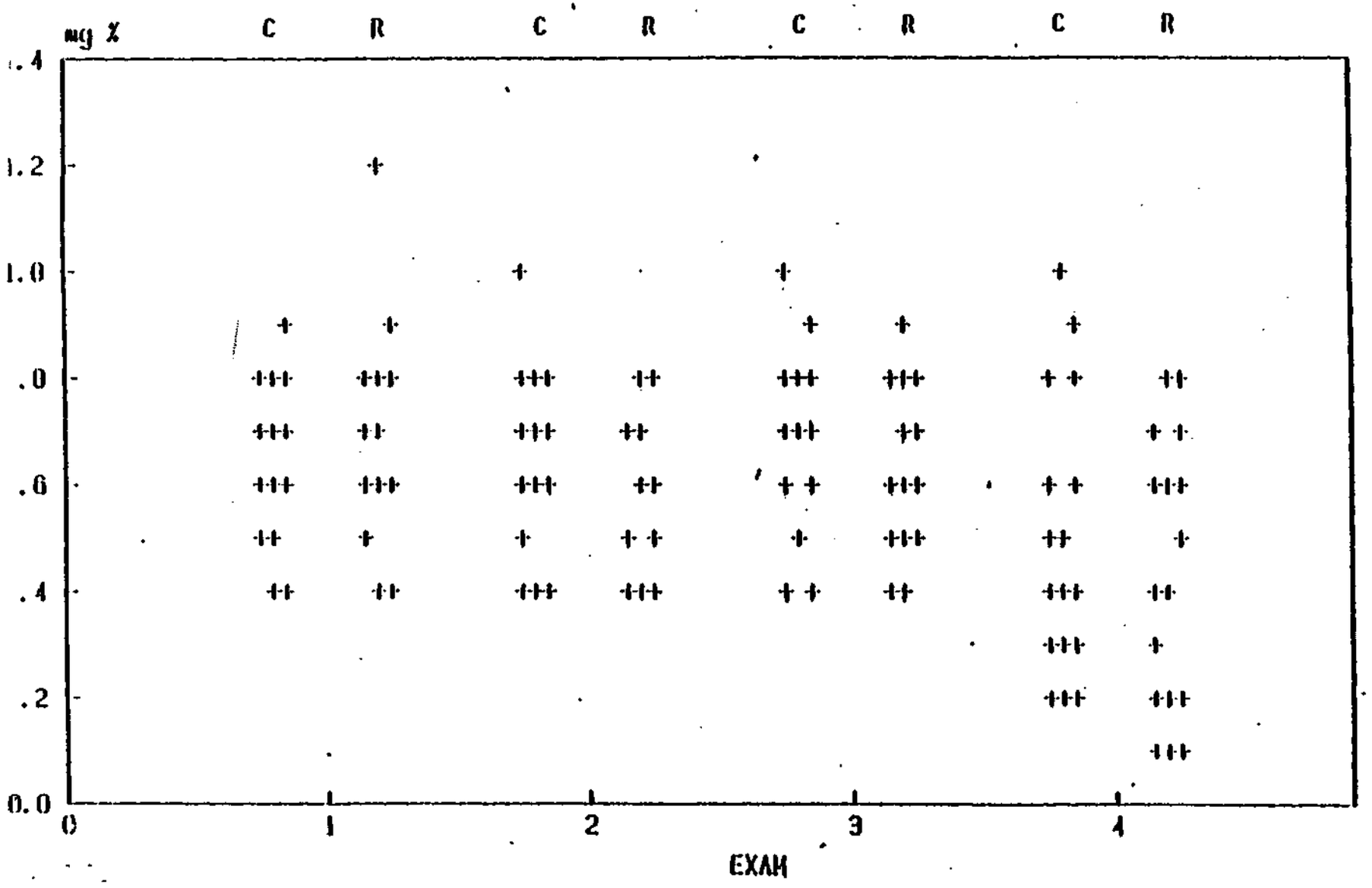
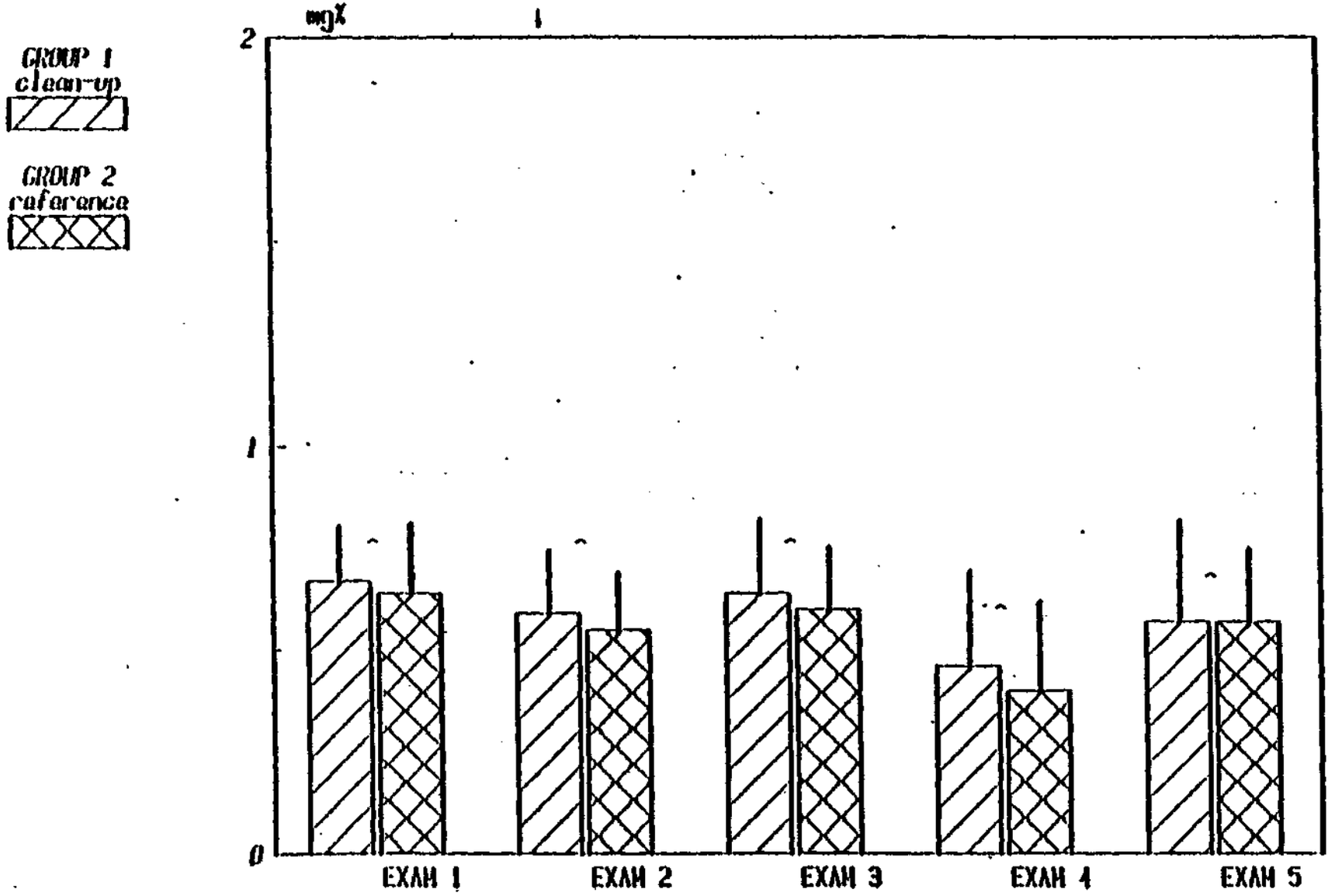


Fig.14 BILIRUBIN (mean+sd)
in clean-up and reference groups



^ Significant between-exams mean difference.

Fig. 15 U - ALA values
in clean-up and reference groups

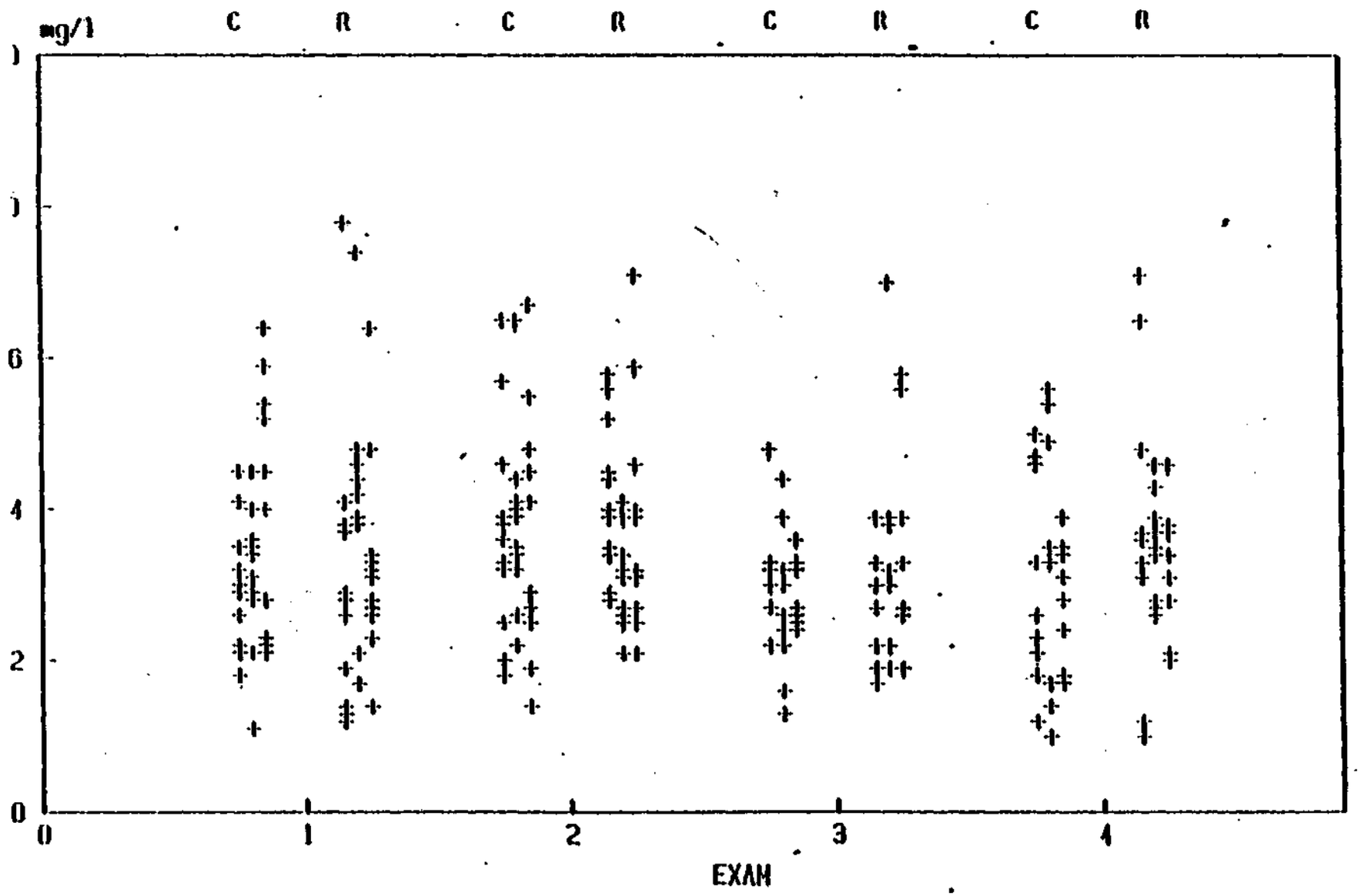
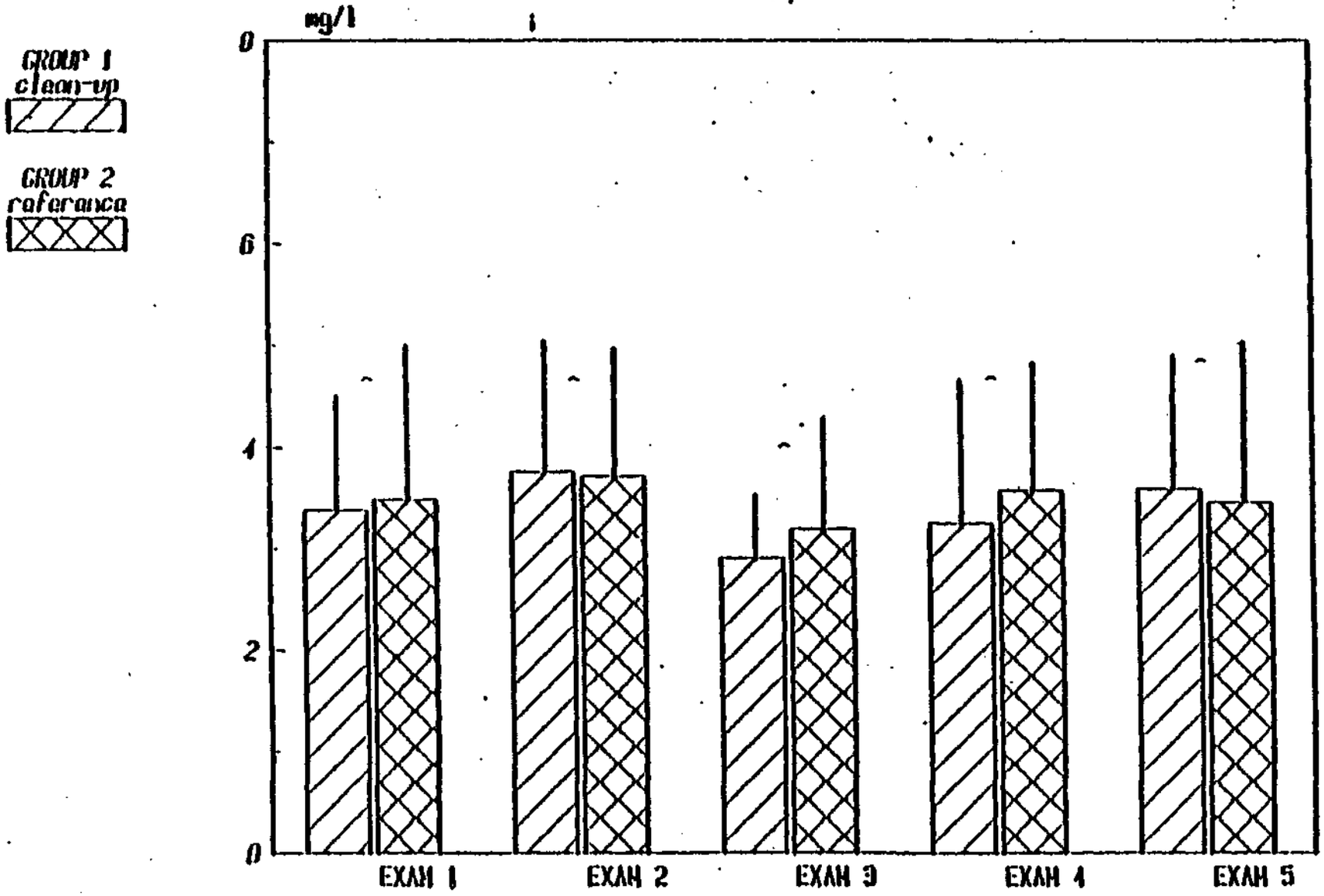


Fig. 16 U - A L A (mean+sd)

in clean-up and reference groups



* Significant between-exam mean difference.

Fig. 17 CHOLESTEROL values
in clean-up and reference groups

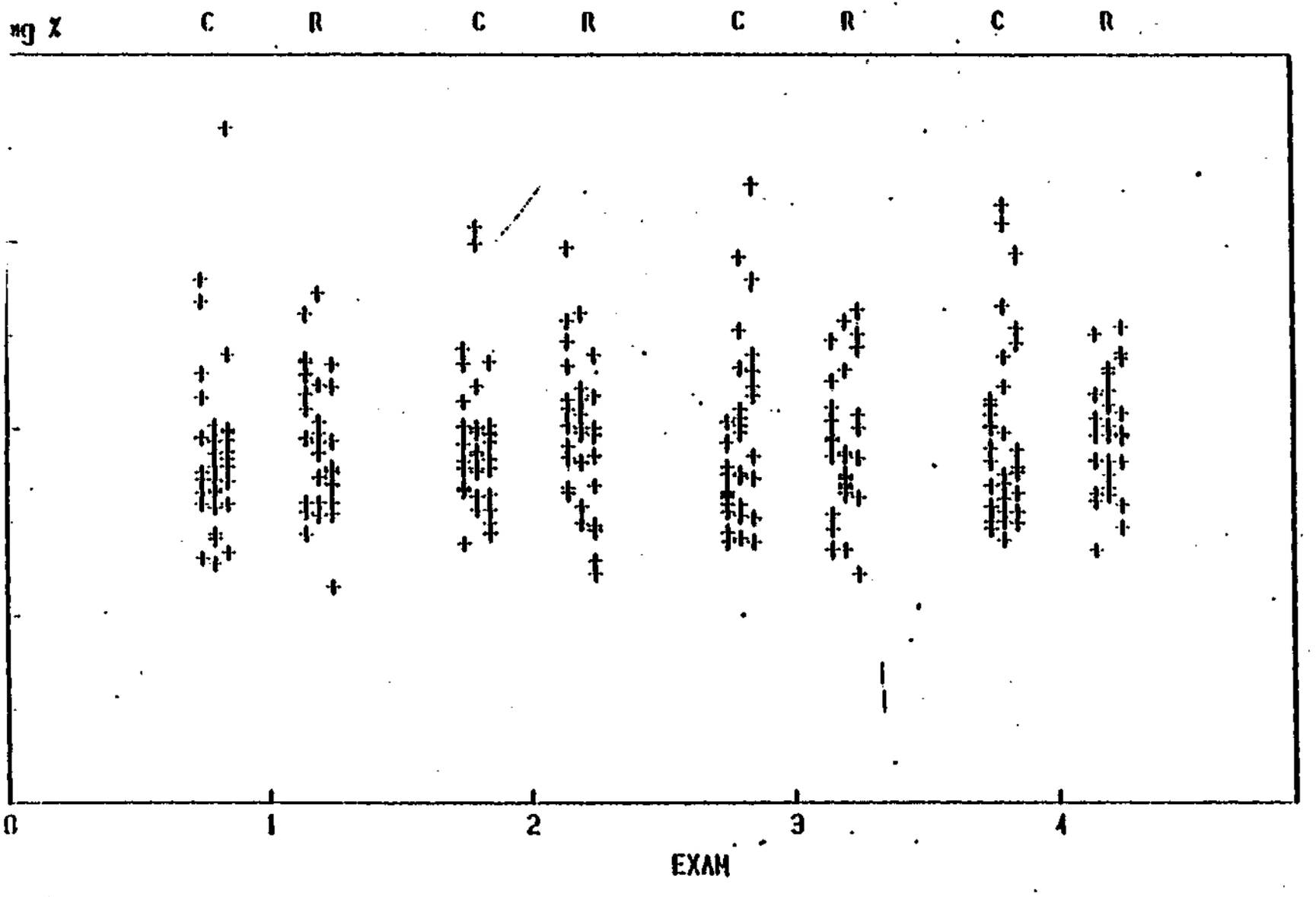


Fig. 18 CHOLESTEROL (mean+sd)

In clean-up and reference groups

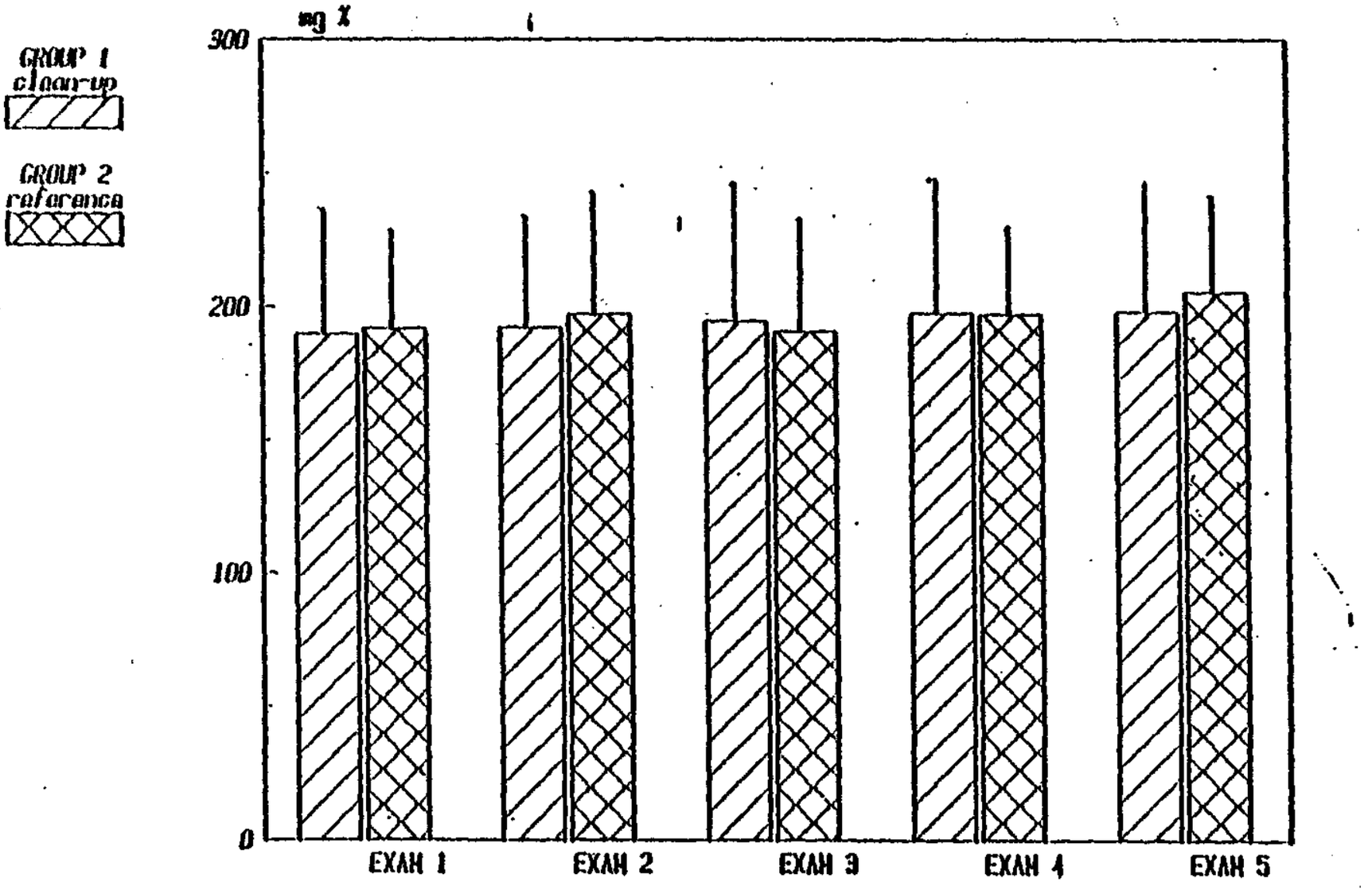


Fig. 19 TRIGLYCERIDES values
in clean-up and reference groups

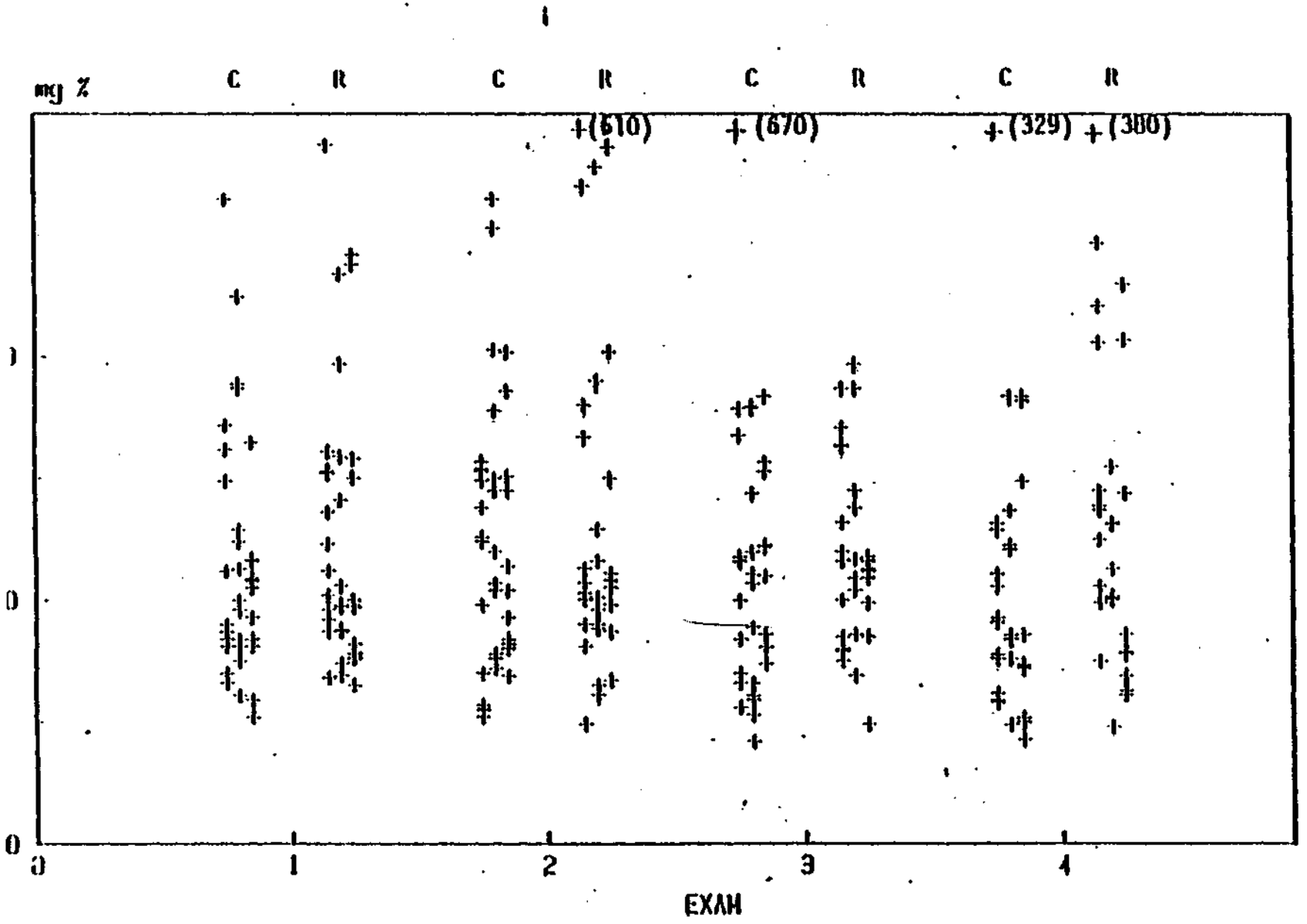


Fig.20 TRIGLYCERIDES (mean+sd)

in clean-up and reference groups

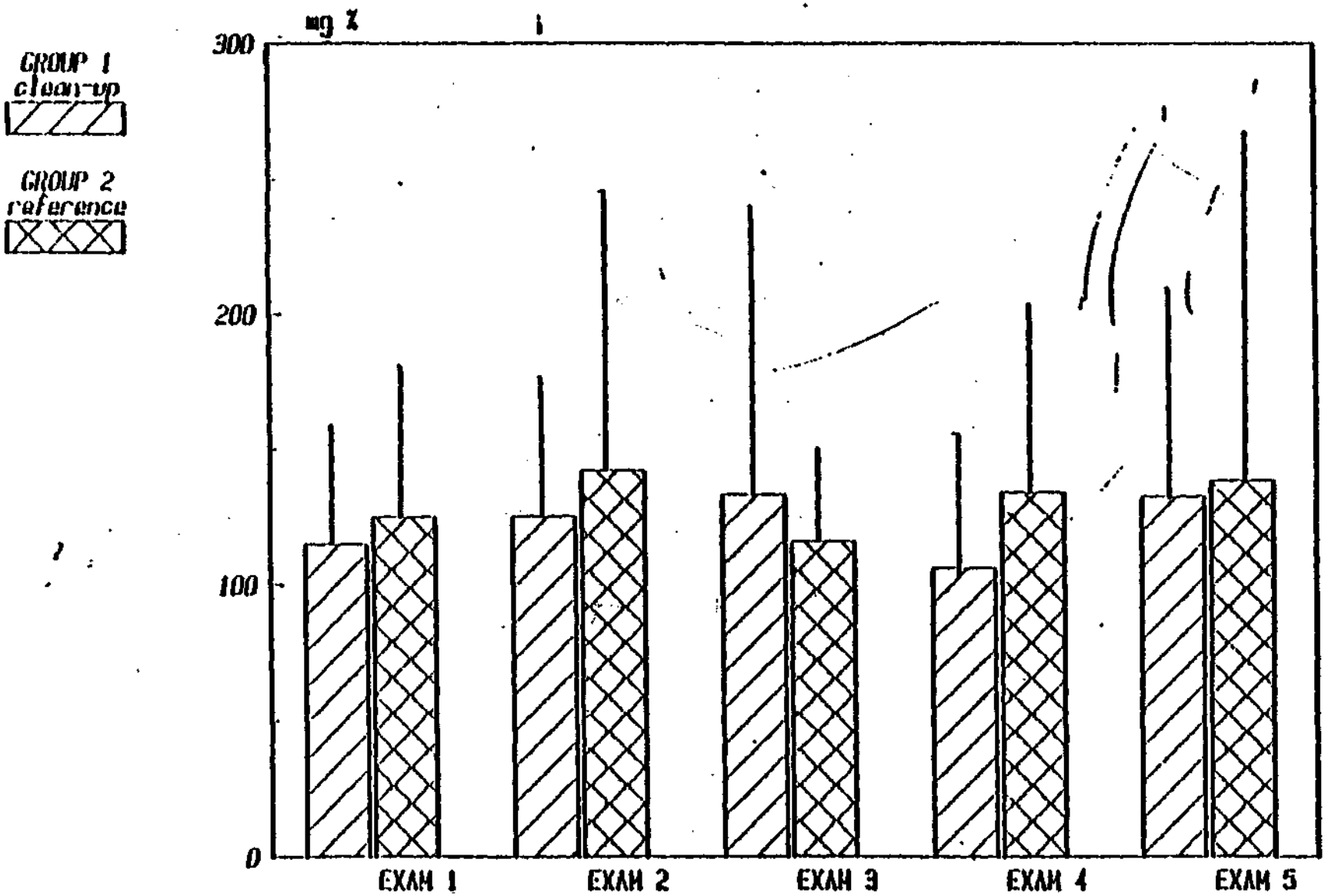


Fig.21 LEUKOCYTES values
in clean-up and reference groups

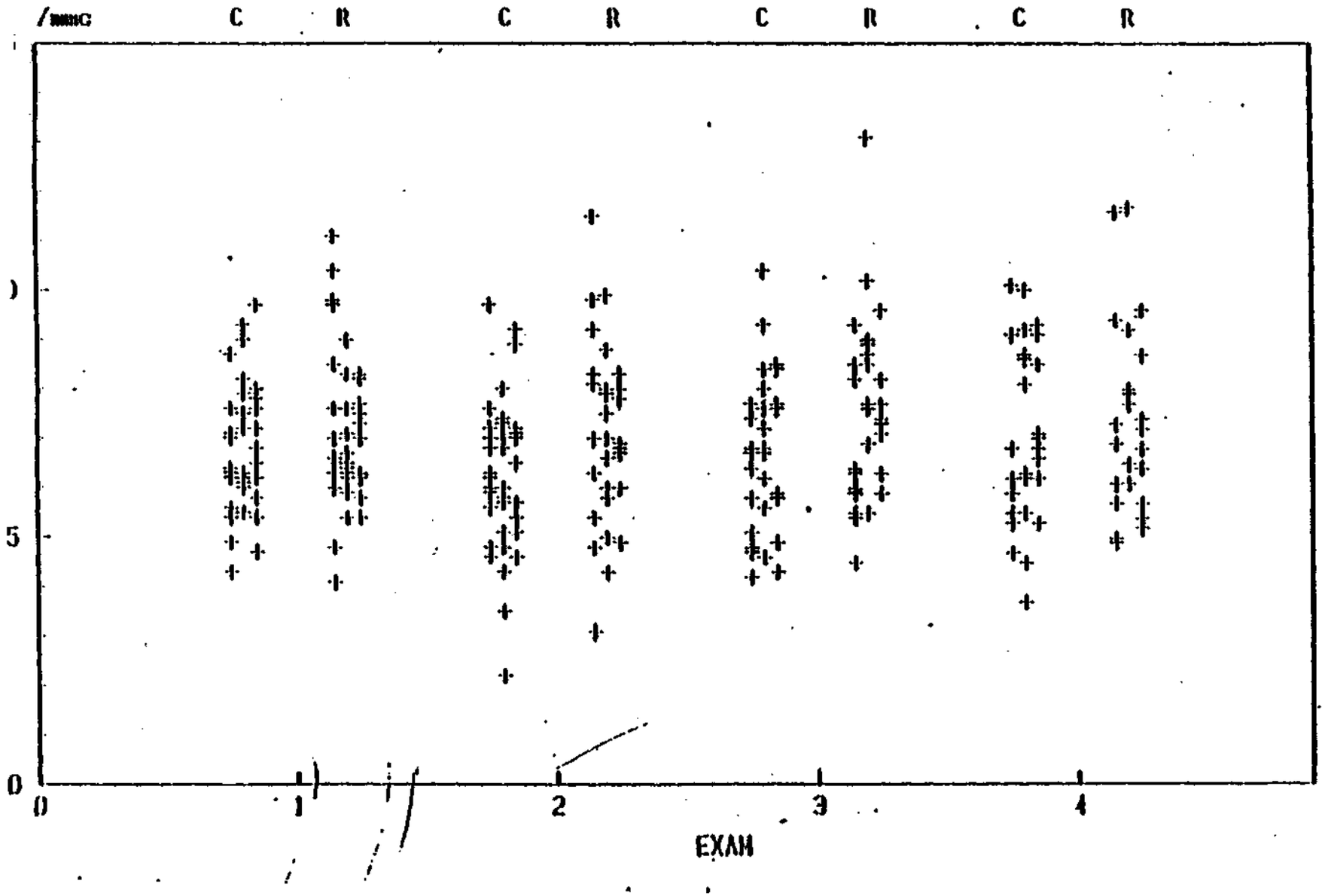
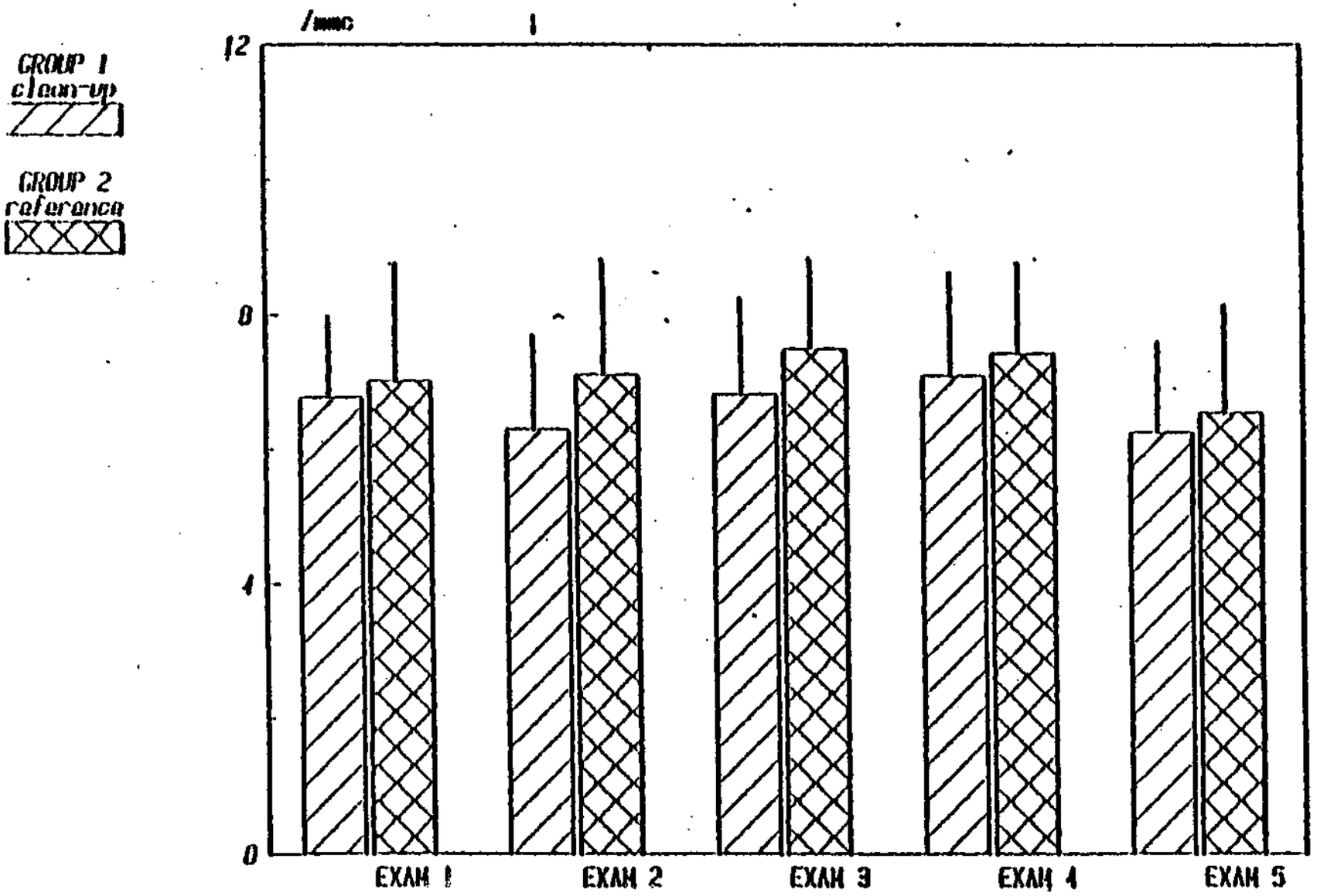
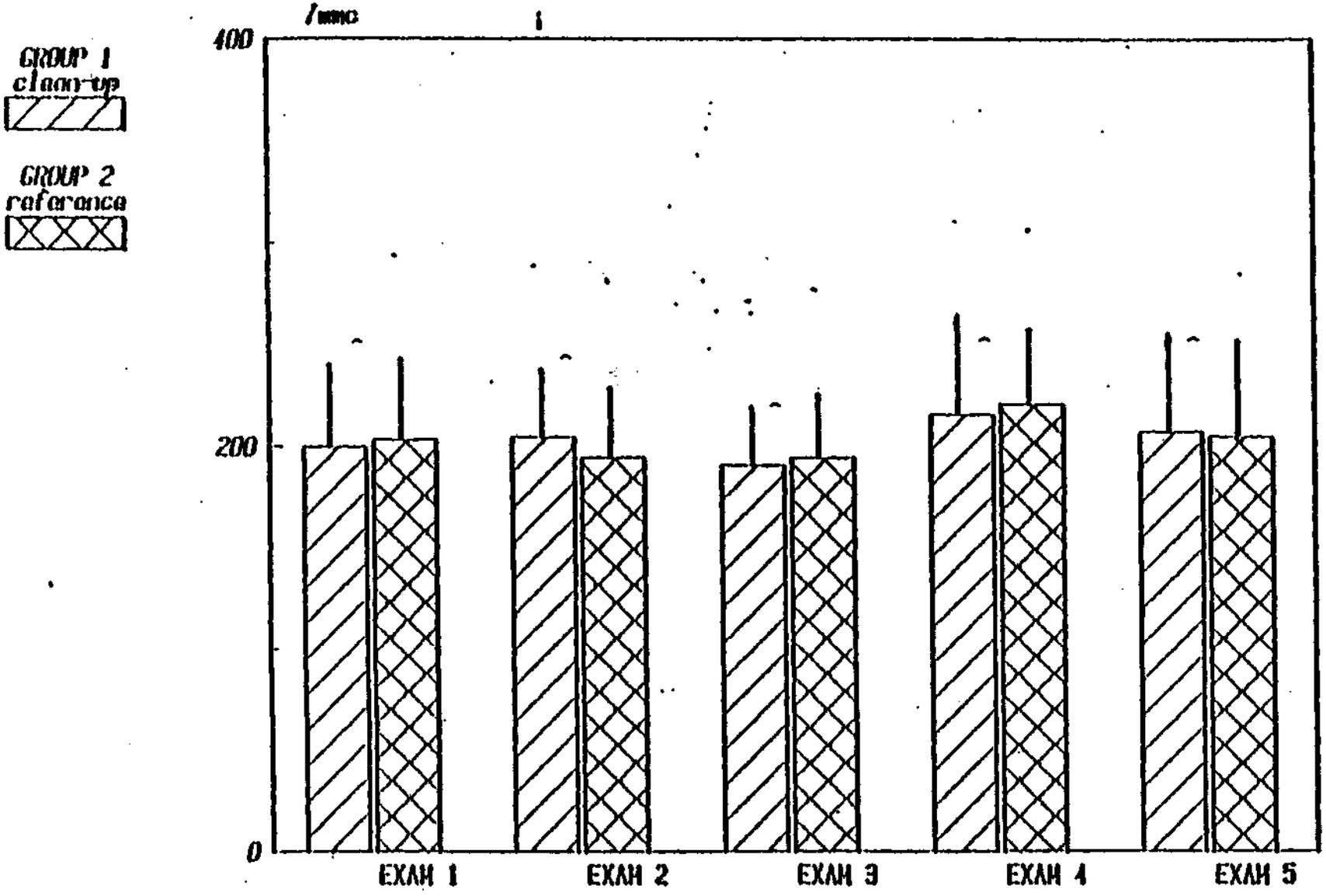


Fig.22 LEUKOCYTES (mean+sd)
in clean-up and reference groups



^ Sinificant between-groups mean difference.

Fig.23 PLATELETS (mean+sd)
in clean-up and reference groups



* Significant between-exams mean difference.

Fig.24 SERUM PROTEINS (mean+sd)

in clean-up and reference groups

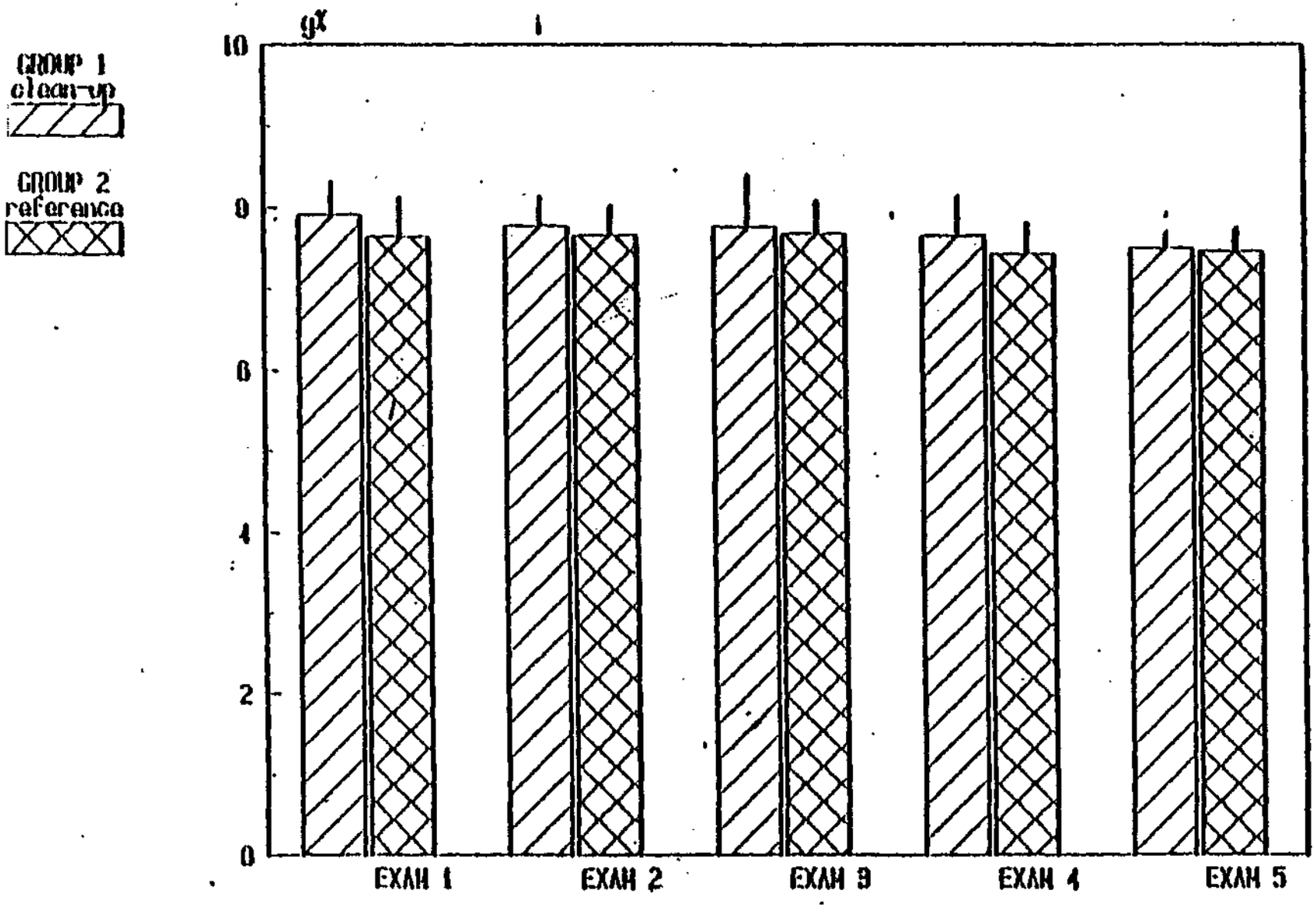


Fig. 25 ALBUMIN (mean+sd)

In clean-up and reference groups

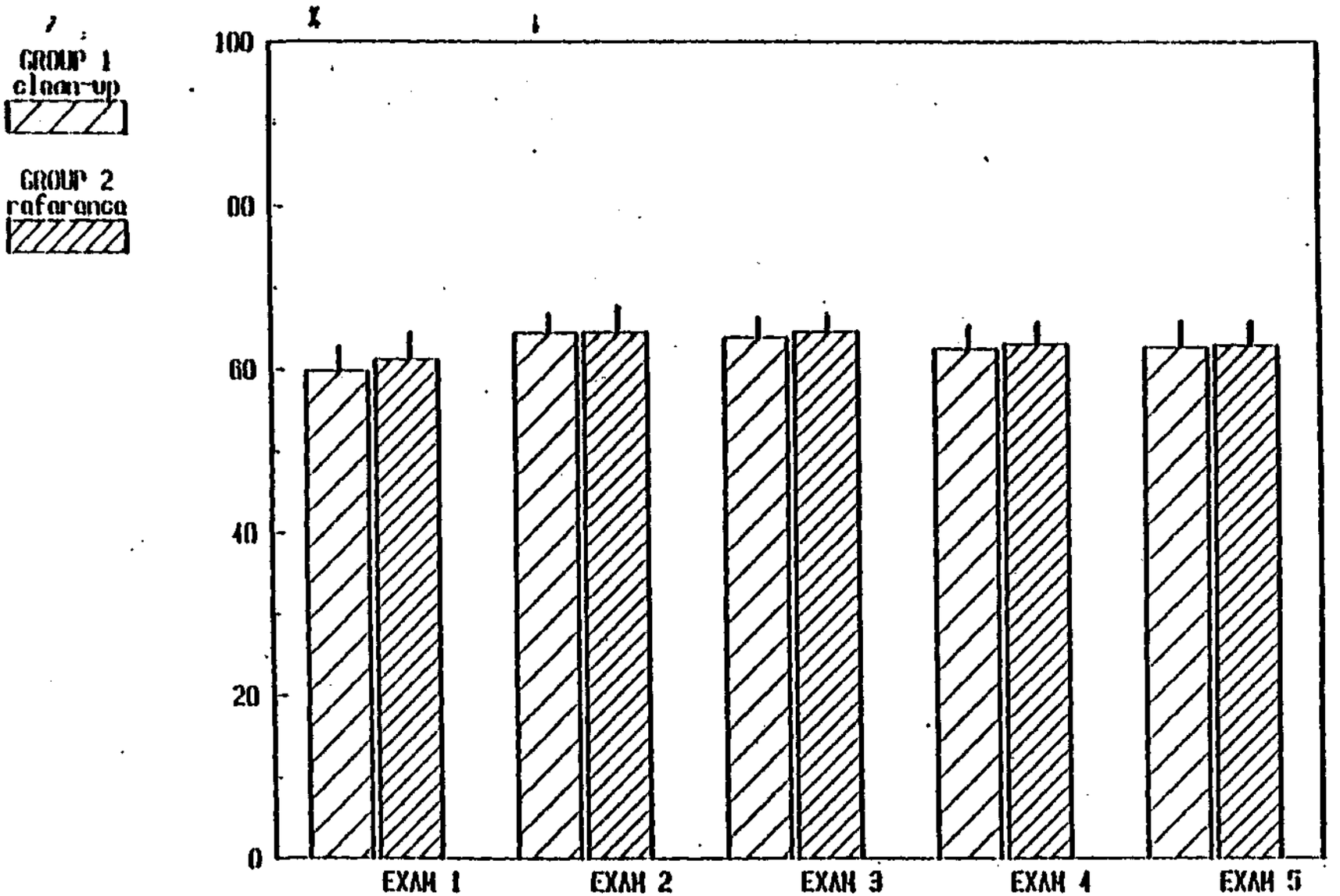
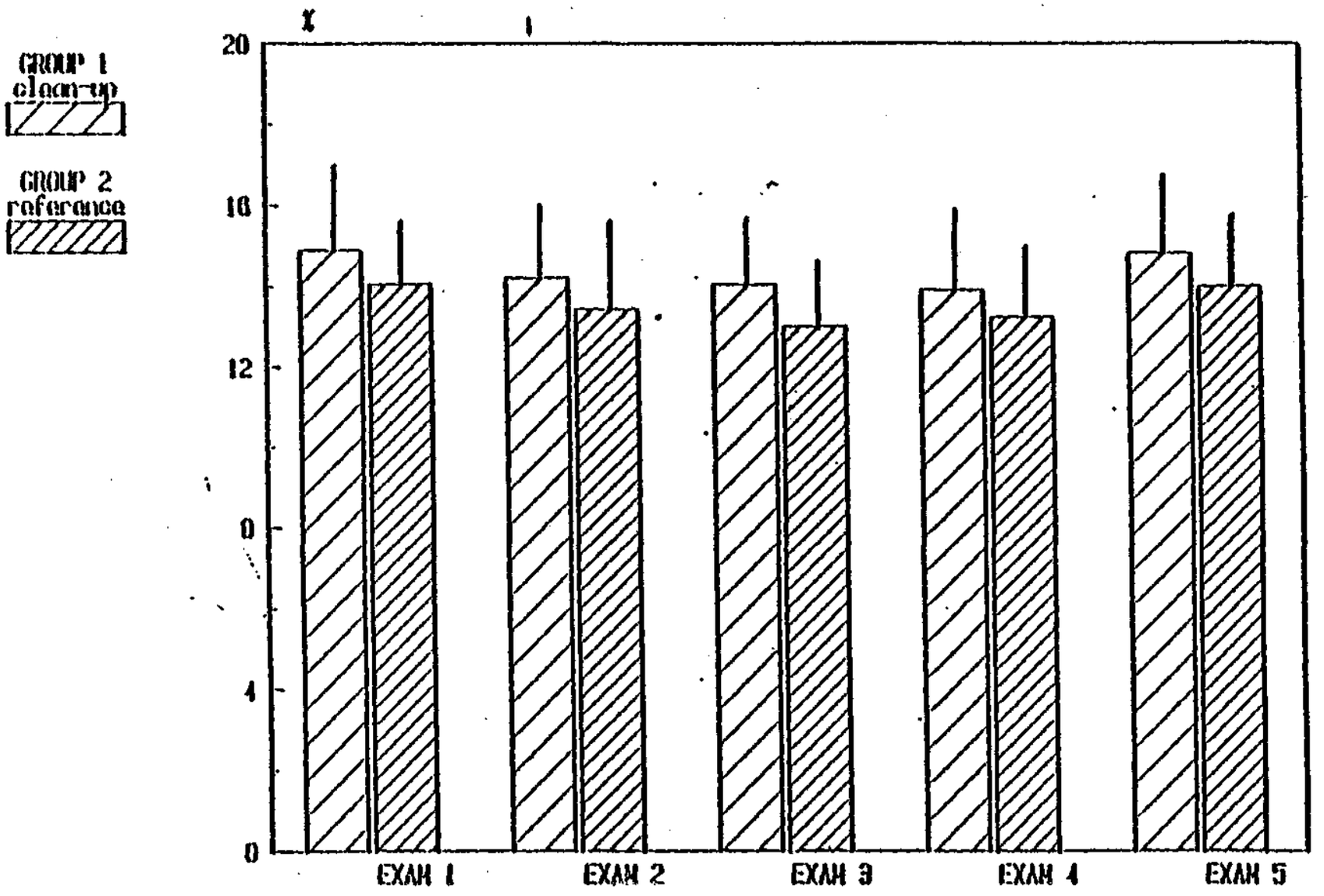


Fig. 26 γ-GLOBULINS (mean+sd)
in clean-up and reference groups



^ Significant between-groups mean difference.

fig. 27 PORPHYRIN PATTERN IN CLEANUP AND CONTROLS, BY EXAM (CUT-OFF=250)

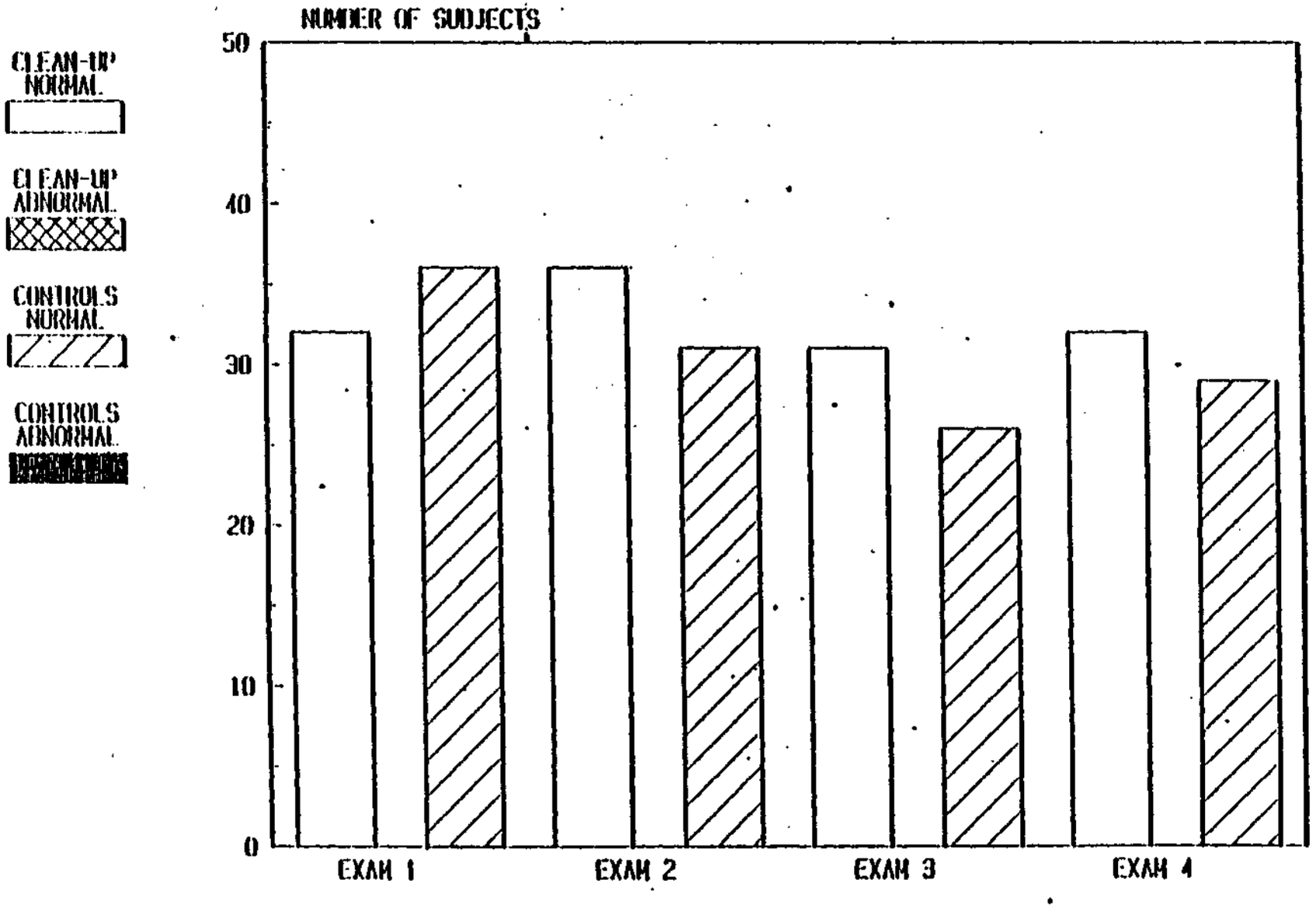


fig.28 SGOT PATTERN IN CLEAN-UP AND CONTROLS, BY EXAM (CUT-OFF=40)

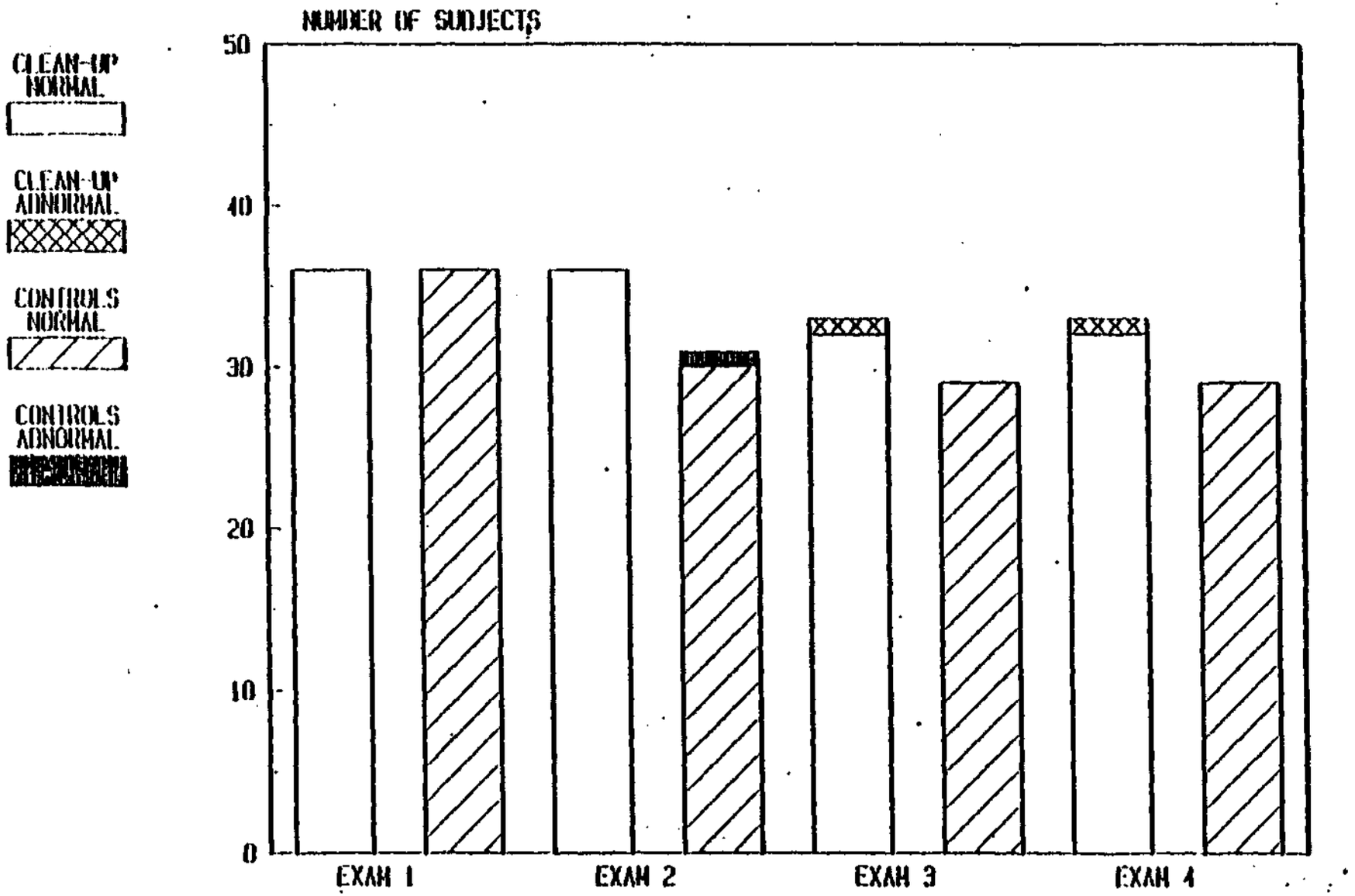


fig. 29 SGPT PATTERN IN CLEAN-UP AND CONTROLS, BY EXAM (CUT-OFF=42)

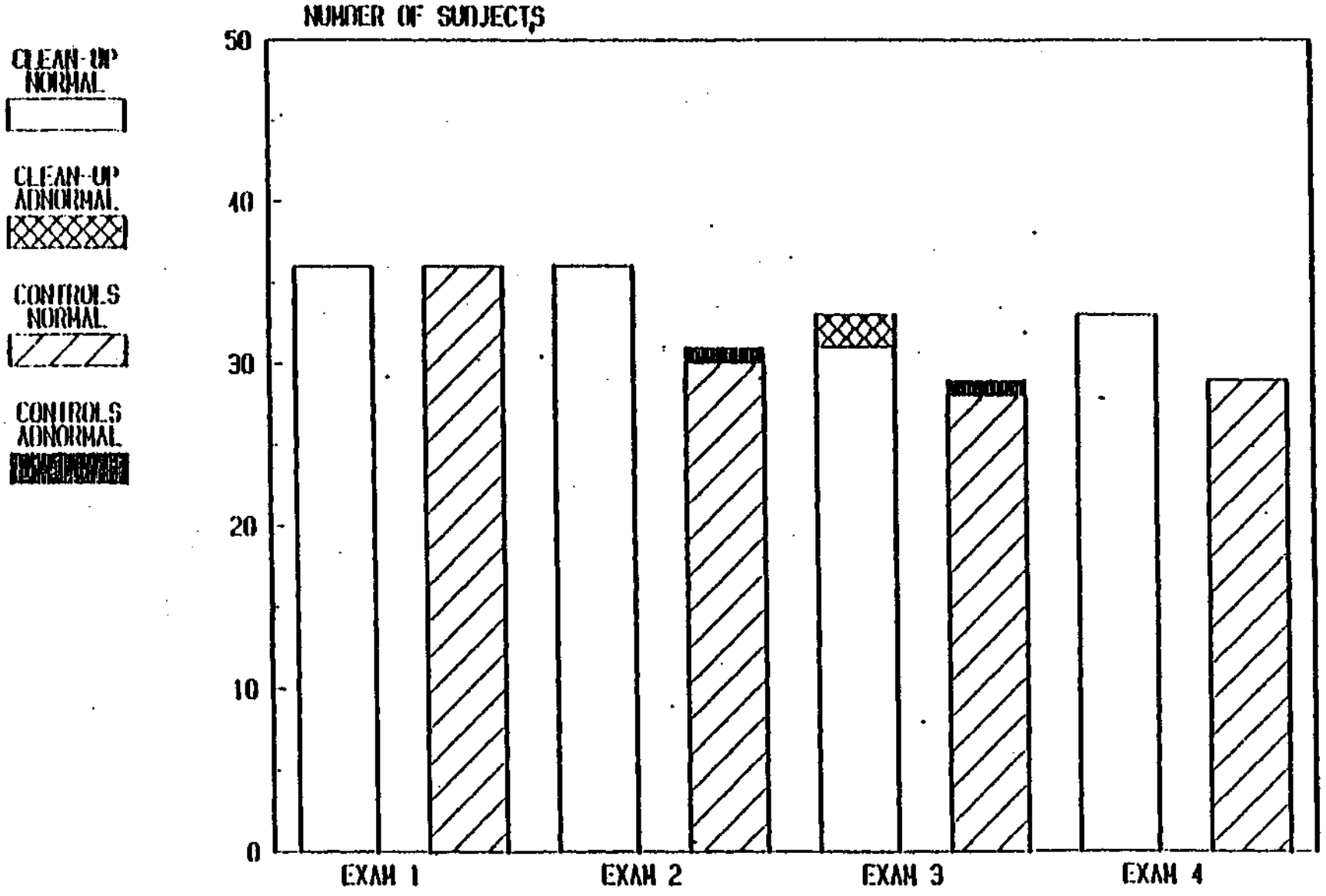


Fig. 30 A. P. PATTERN IN CLEANUP AND CONTROLS, BY EXAM (CUT-OFF=50)

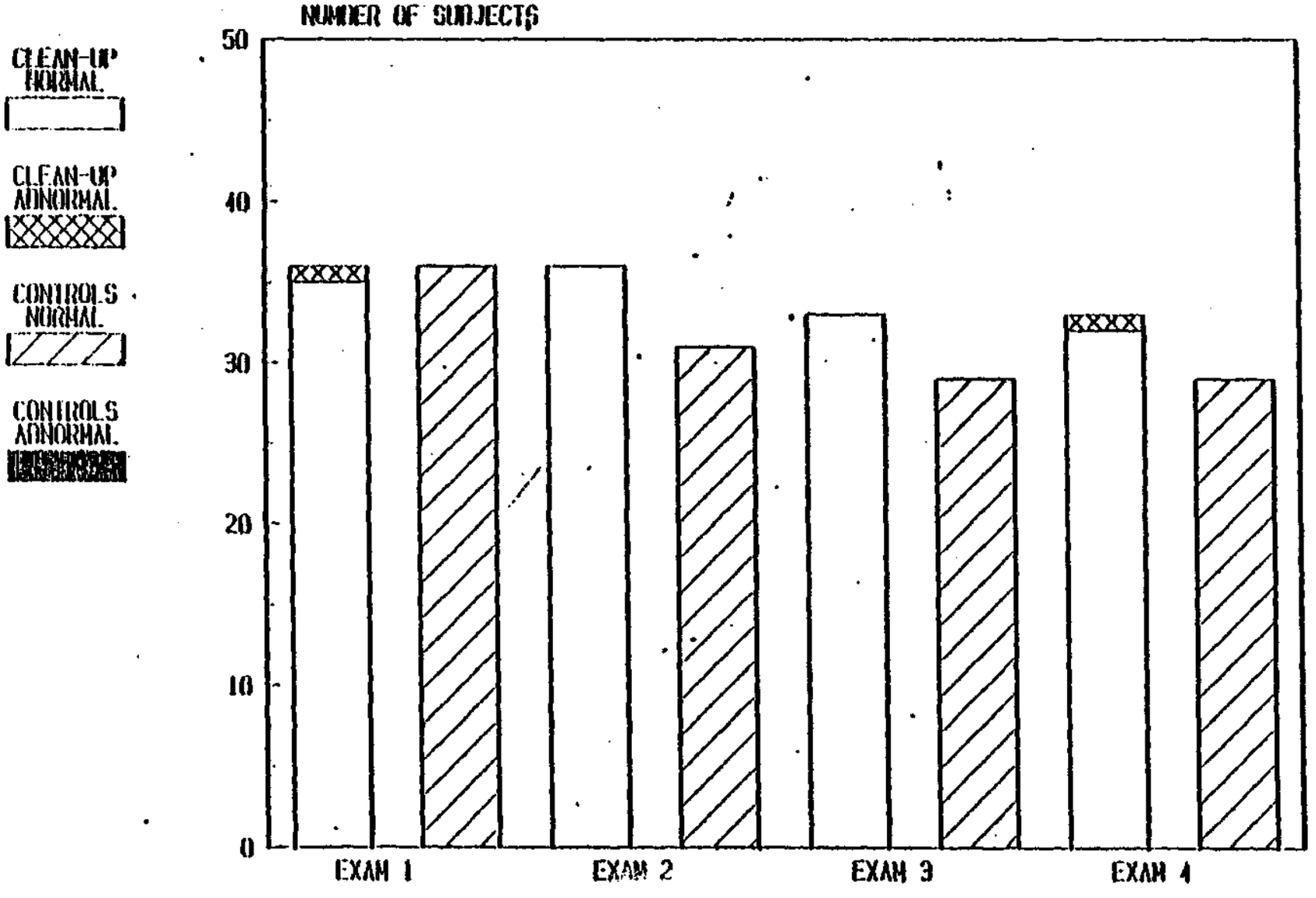


Fig. 31 GGTP-PATTERN IN CLEANUP AND CONTROLS, BY EXAM (CUT-OFF=50)

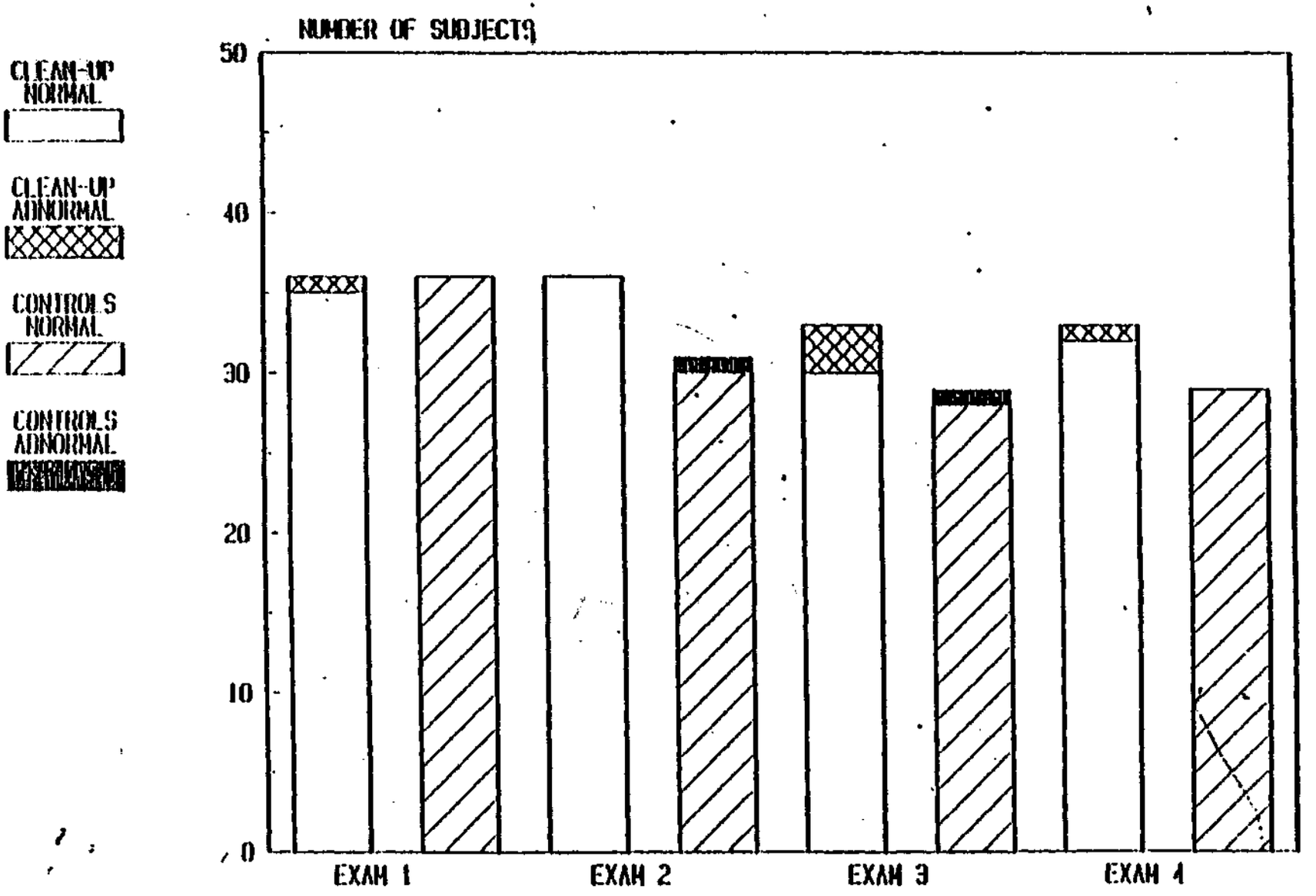


Fig.32 BILIRUBIN IN CLEAN-UP AND CONTROLS, BY EXAM (CUT-OFF=1.4)

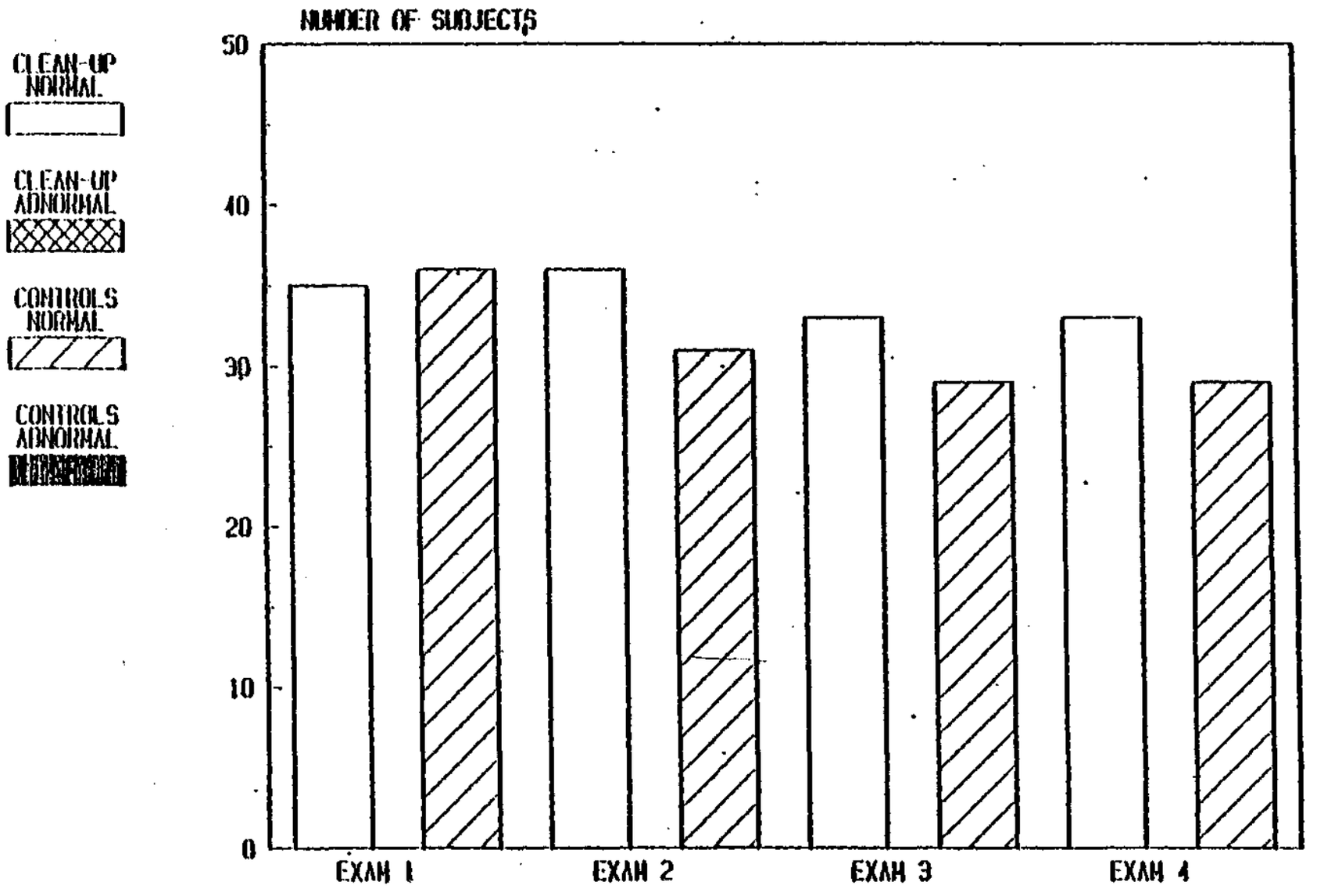


Fig.33 WBC PATTERN IN CLEAN-UP AND CONTROLS, BY EXAM (CUTOFF=3.5)

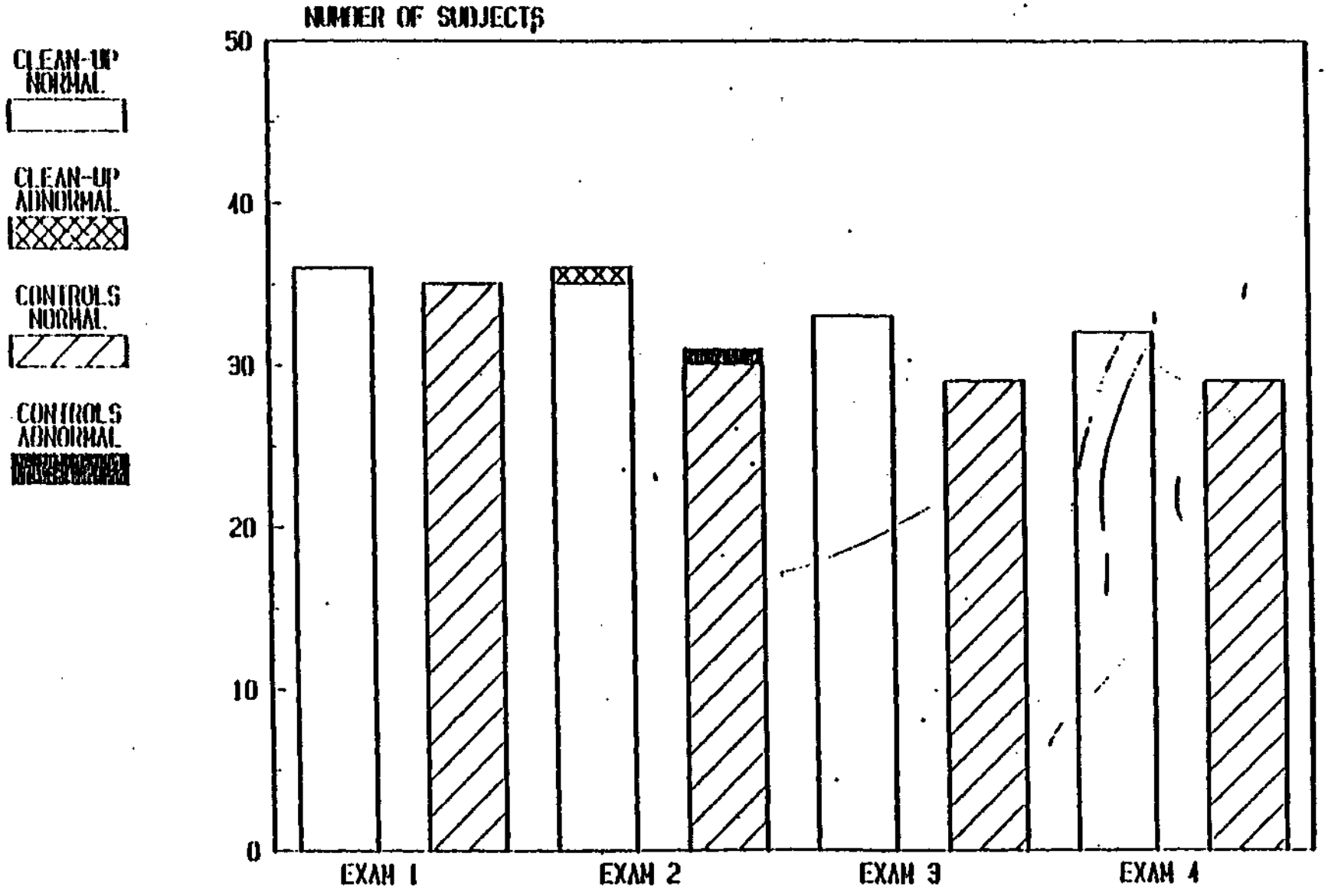


Fig.34 U - ALA PATTERN IN CLEAN-UP AND CONTROLS, BY EXAM (CUT-OFF=6)

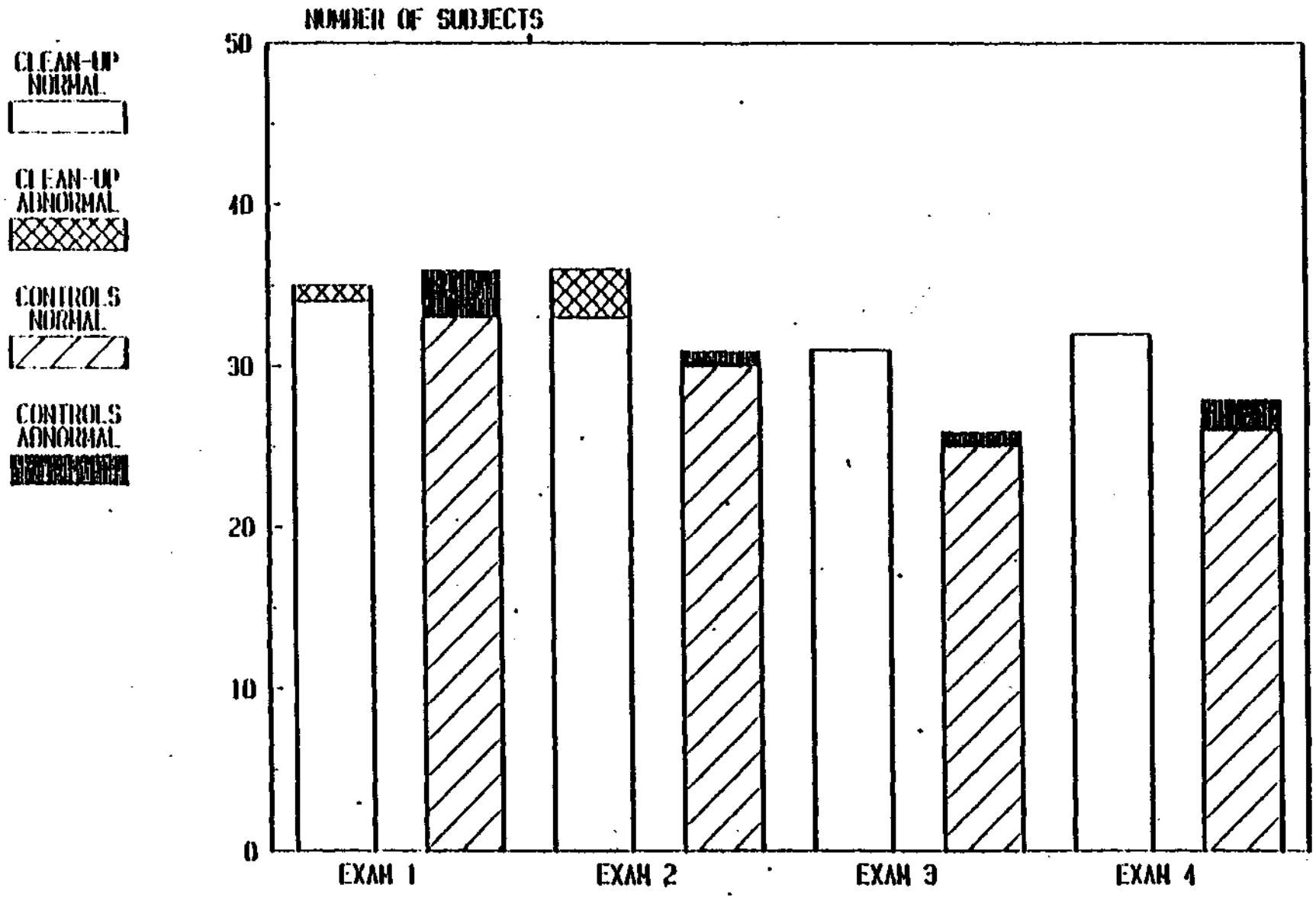


Fig. 35 CHOLESTEROL IN CLEANUP AND CONTROLS, BY EXAM (CUTOFF=270)

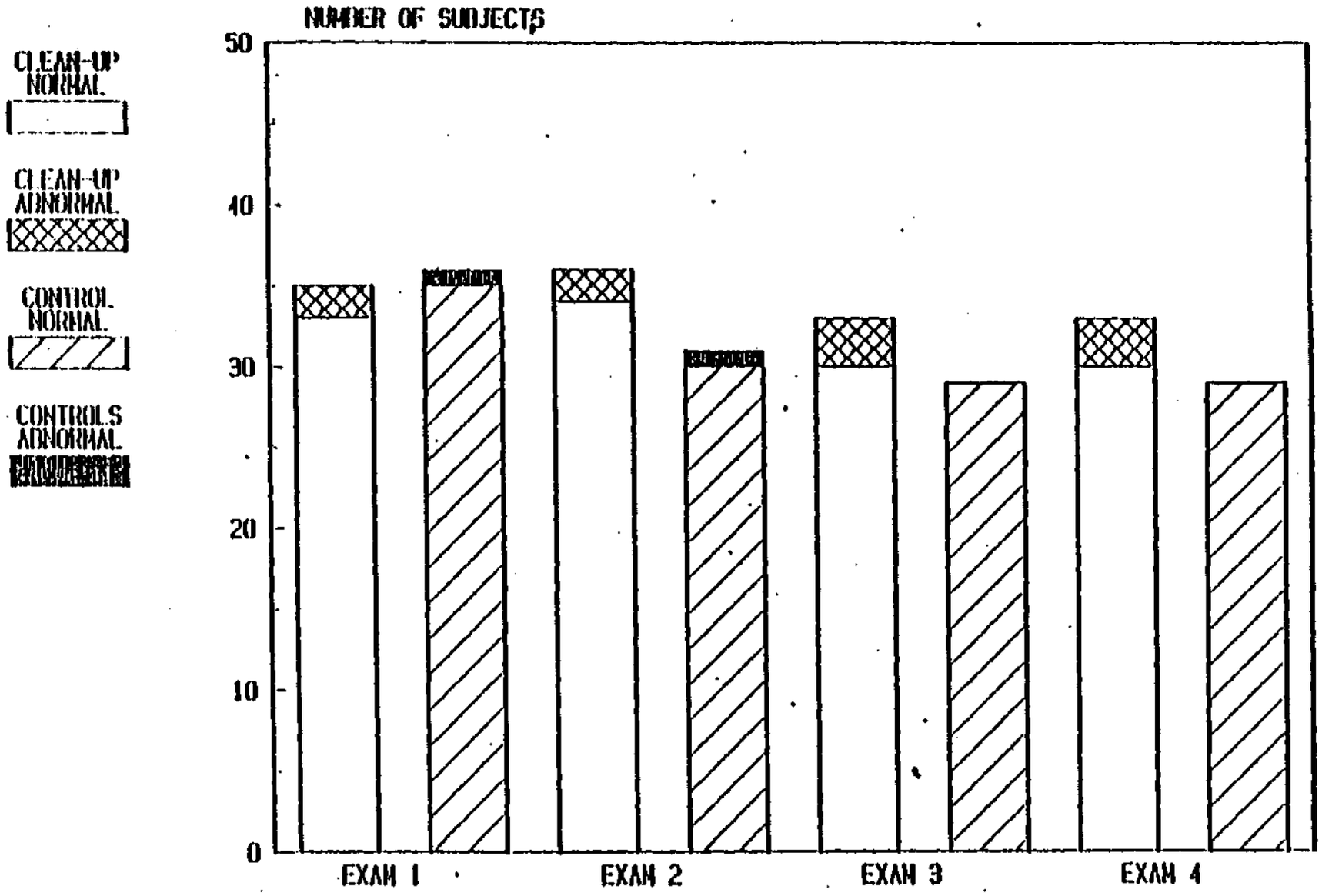
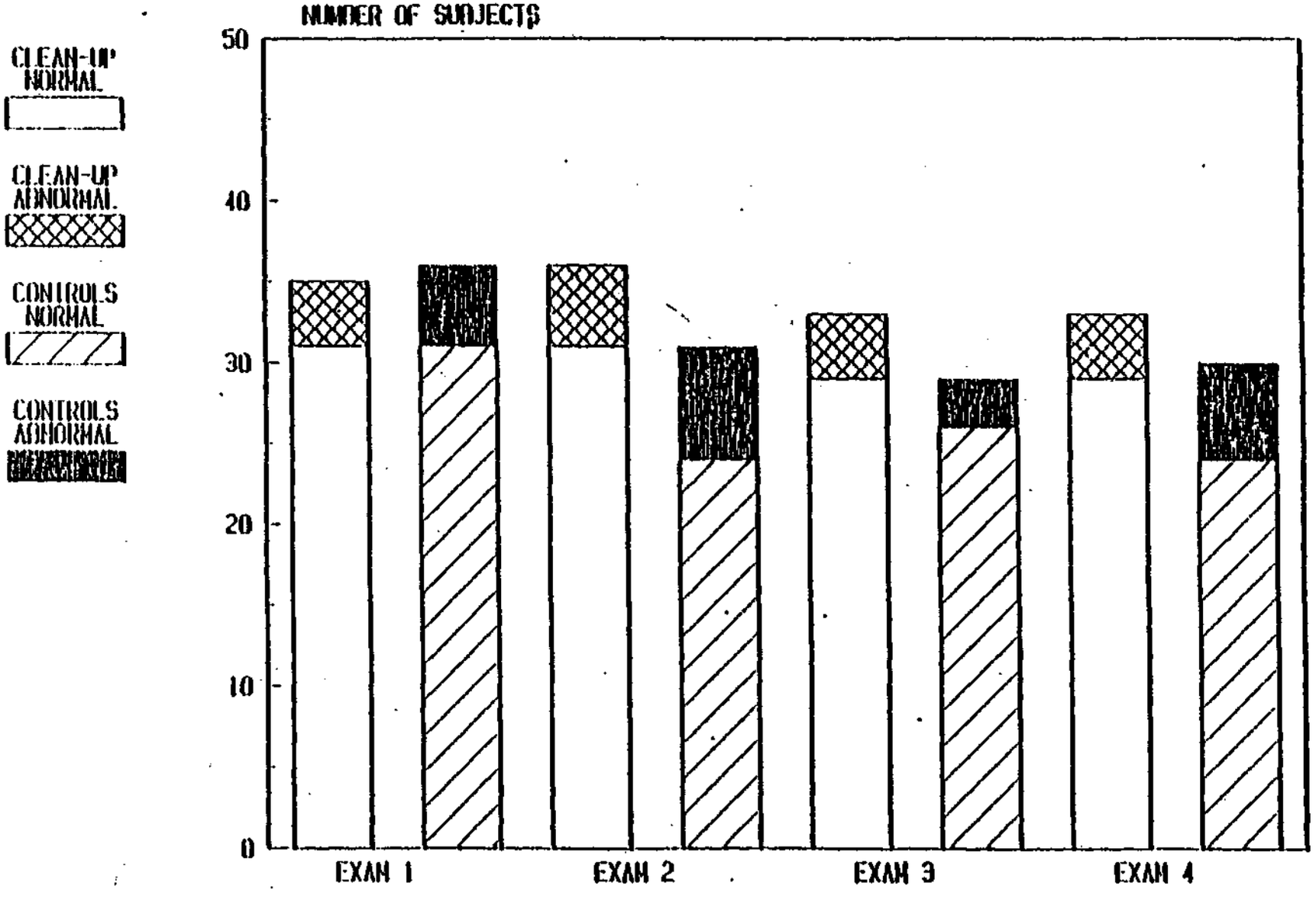


Fig. 36 TRIGLYC. IN CLEAN-UP AND CONTROLS, BY EXAM (CUT-OFF=180)



ON 13 LABORATORY TESTS IN CLEAN-UP AND REFERENCE GROUPS, BY EXAM.

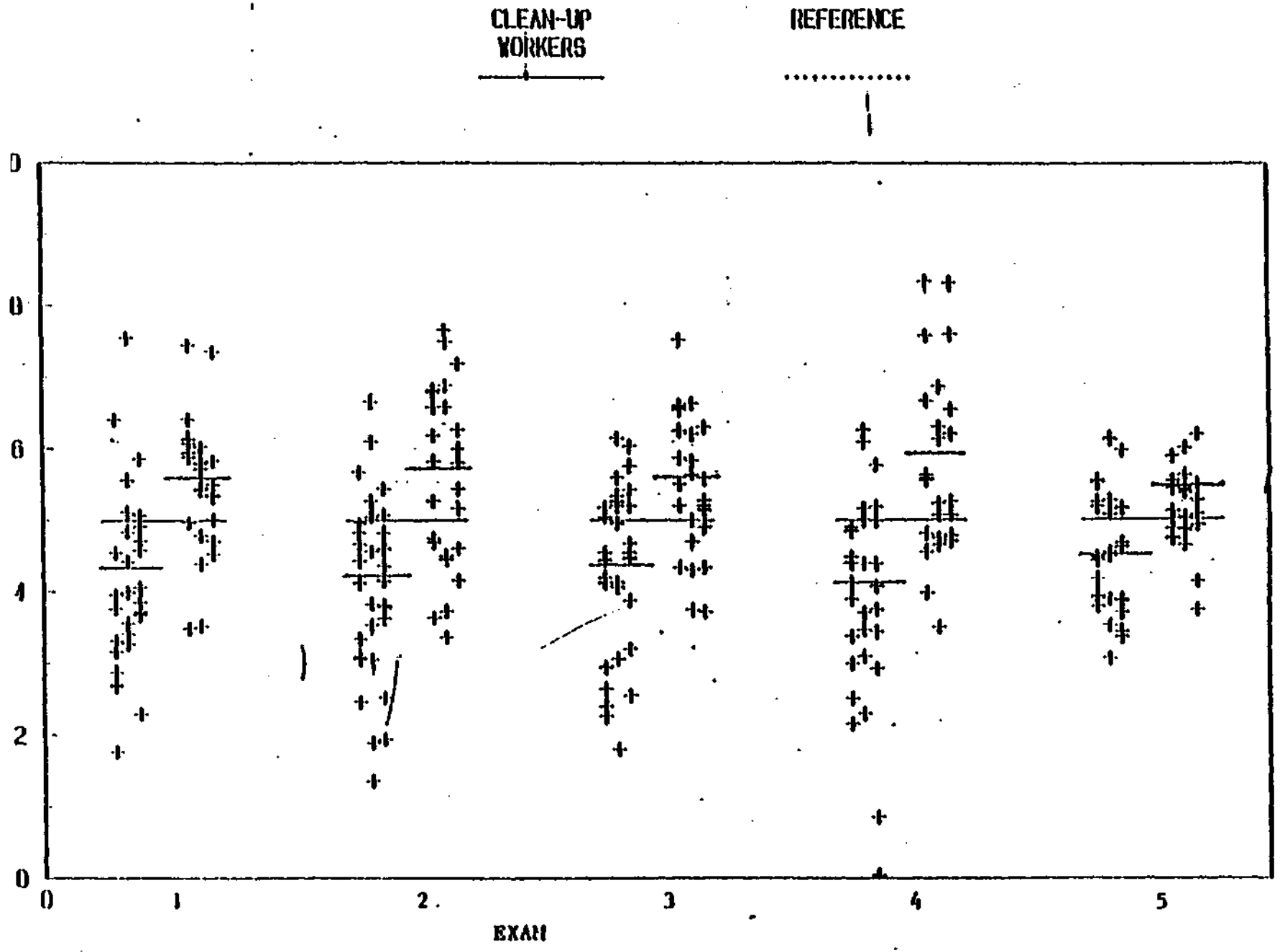


Fig.38 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER # 1: S.P., 25 yrs

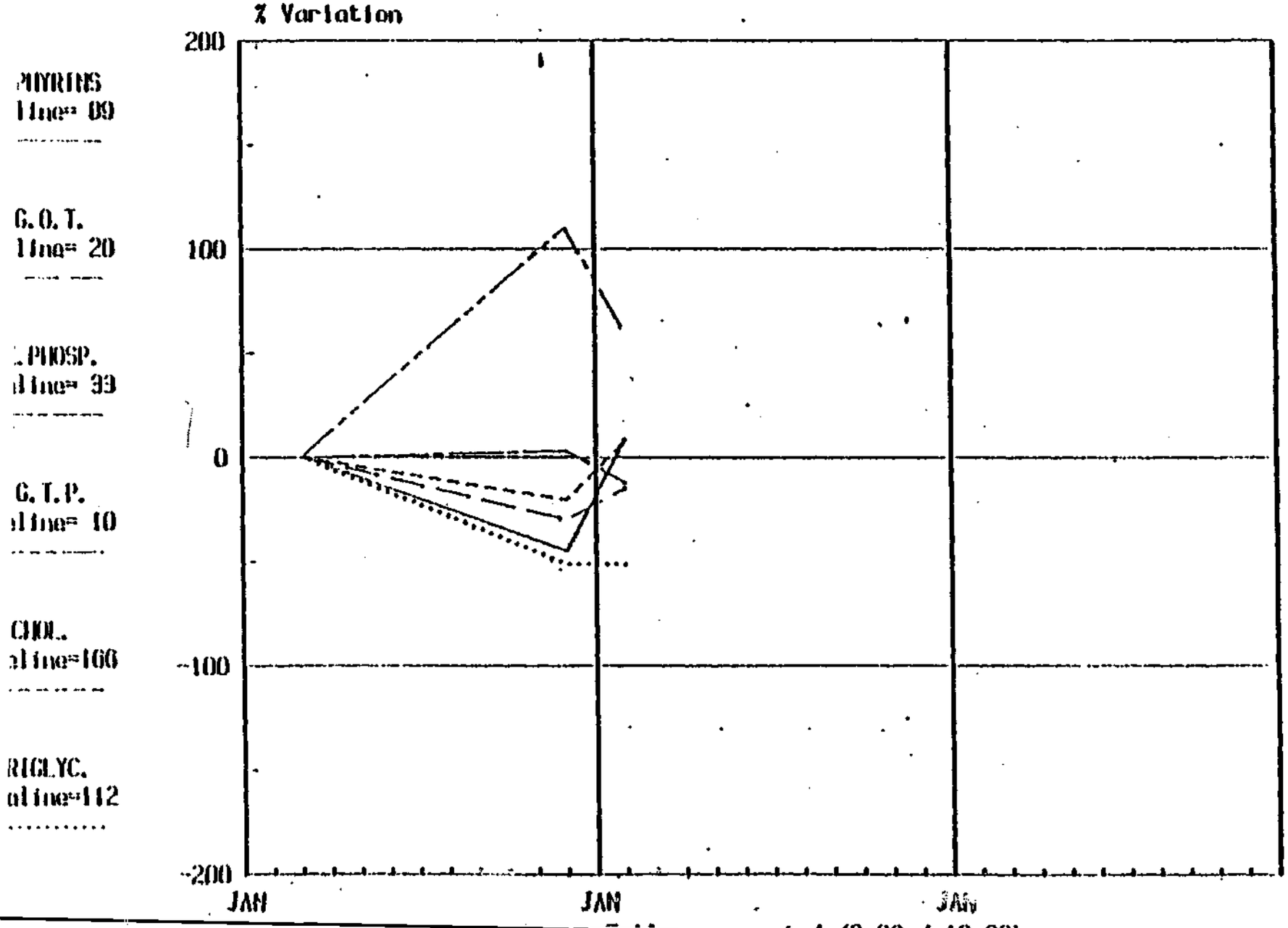


Fig. 39 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER # 2: G.G., 32 yrs

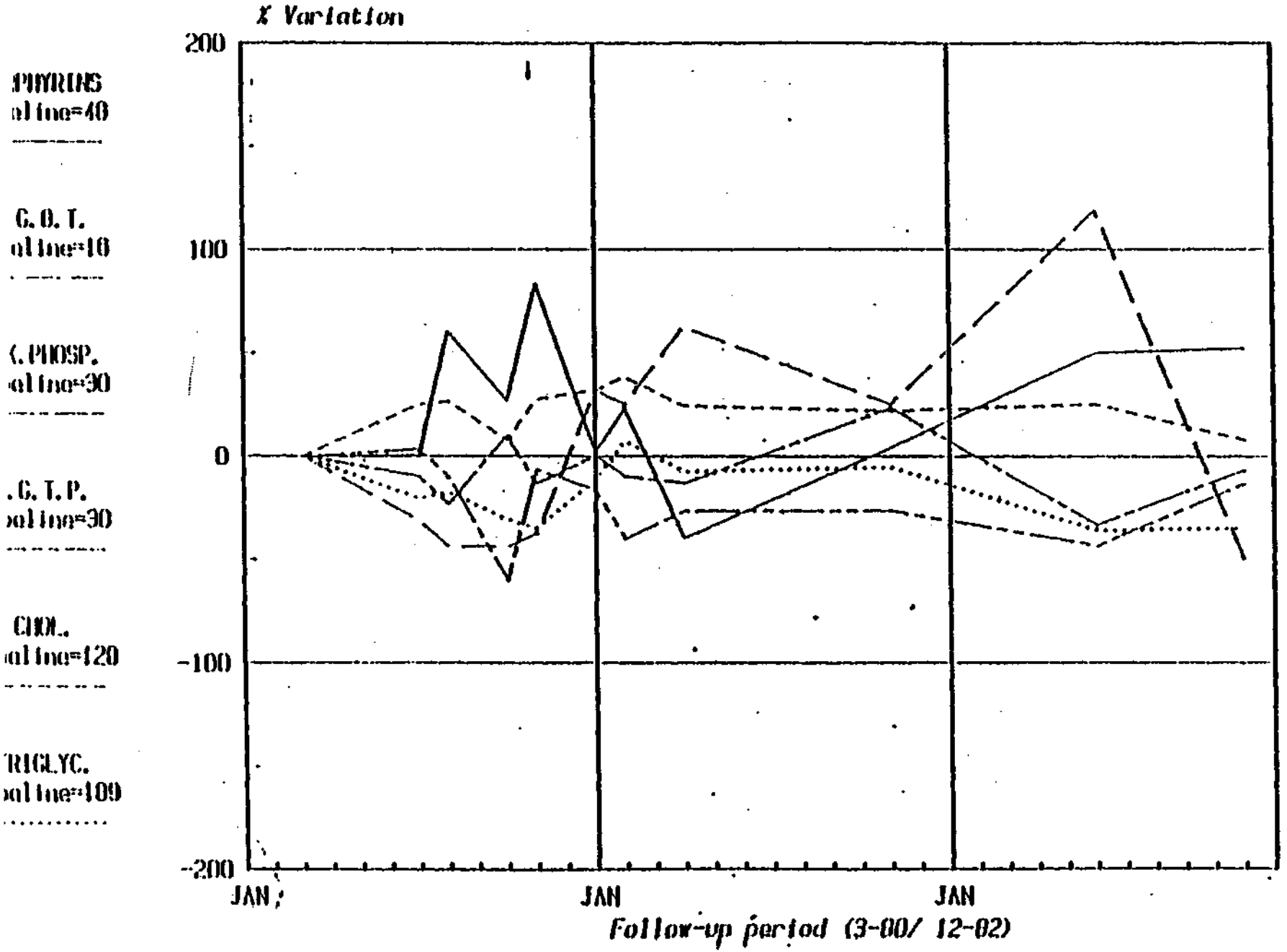


Fig. 40 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #3: V.F., 39 yrs

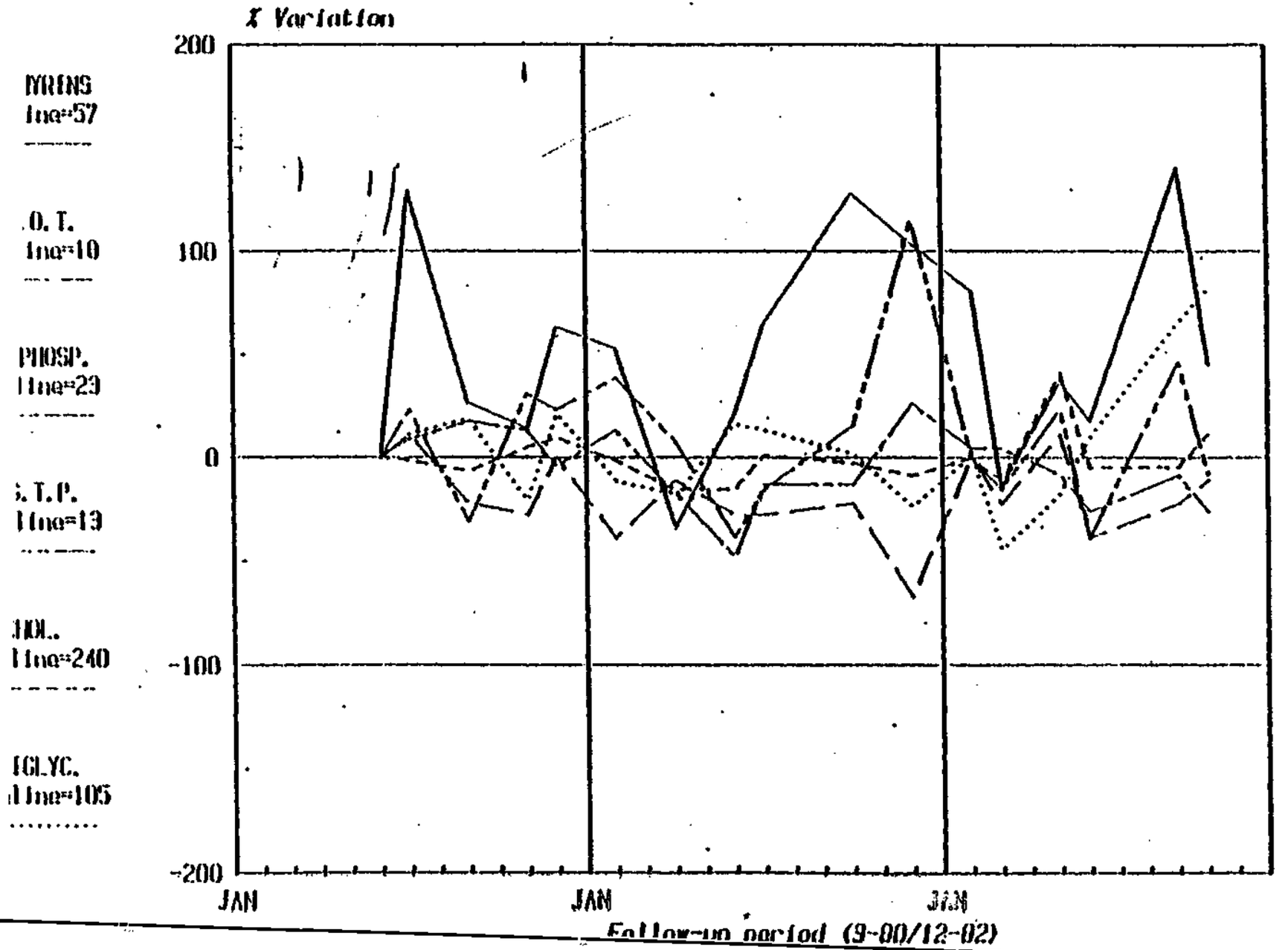


Fig.41: TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER # 4: P.V., 34 yrs

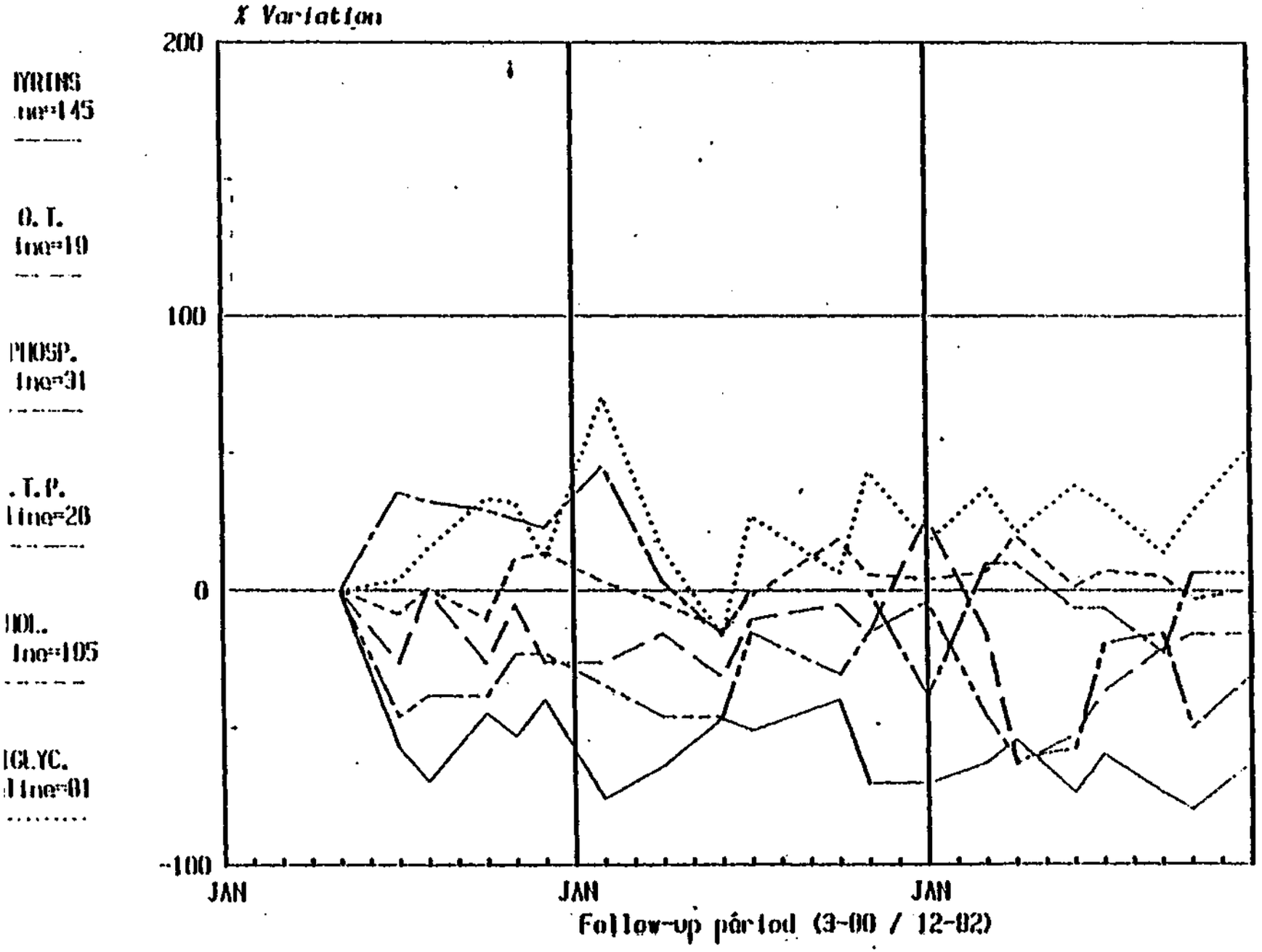


Fig. 42: TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #5: I.S., 41 yrs

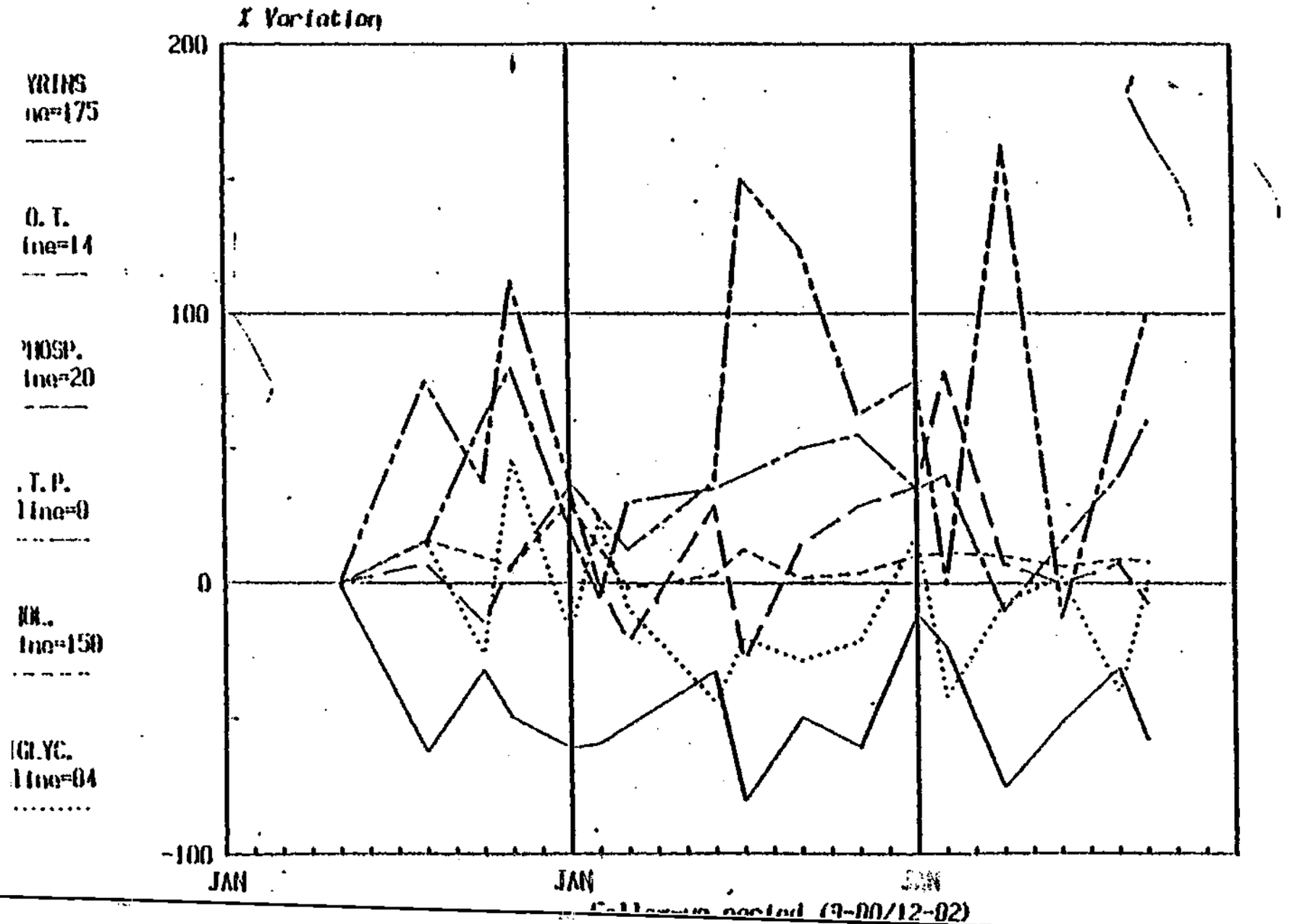


Fig. 43 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #6: V.C., 27 yrs

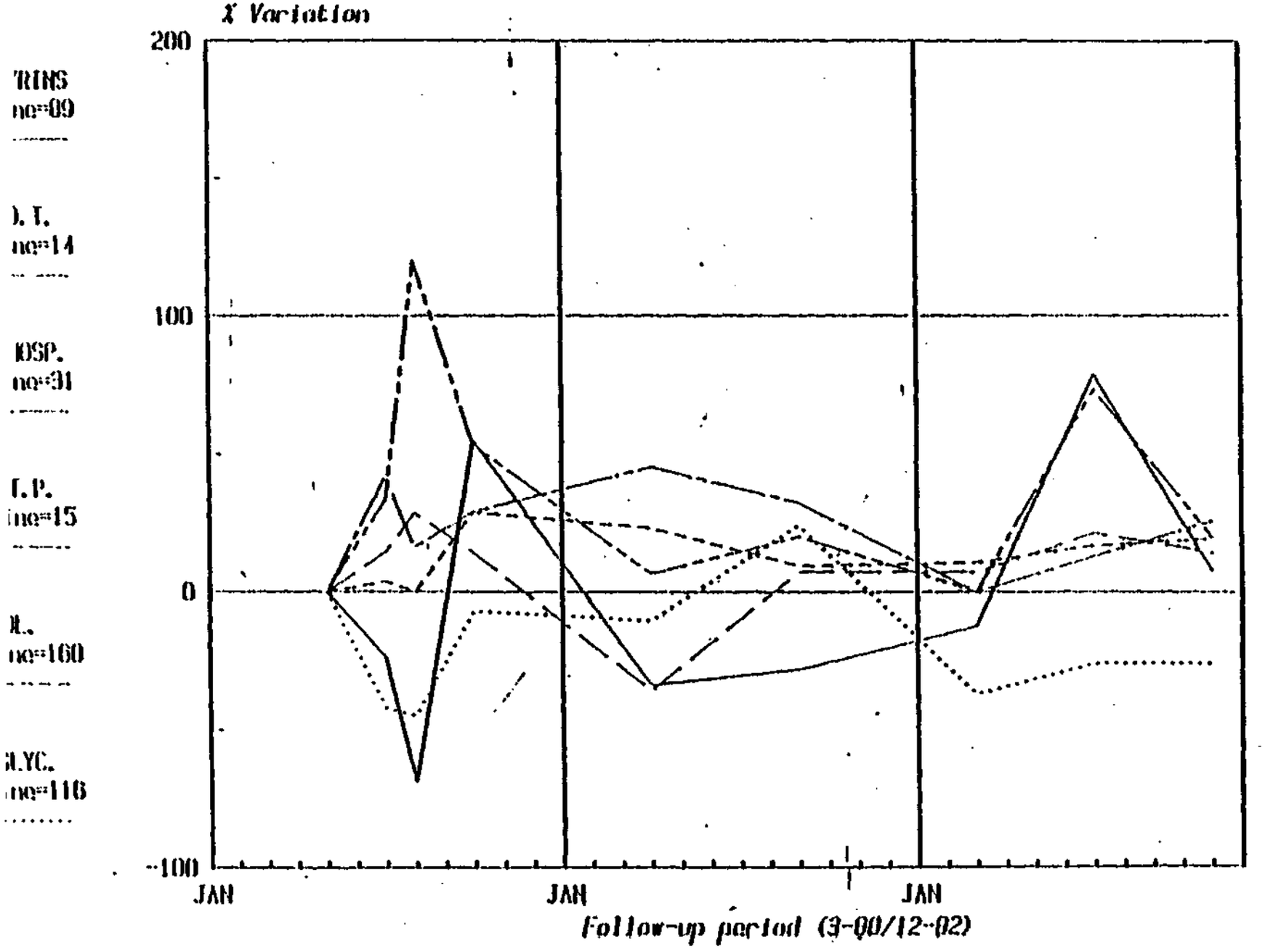


Fig. 44 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #7: G.N., 26 yrs

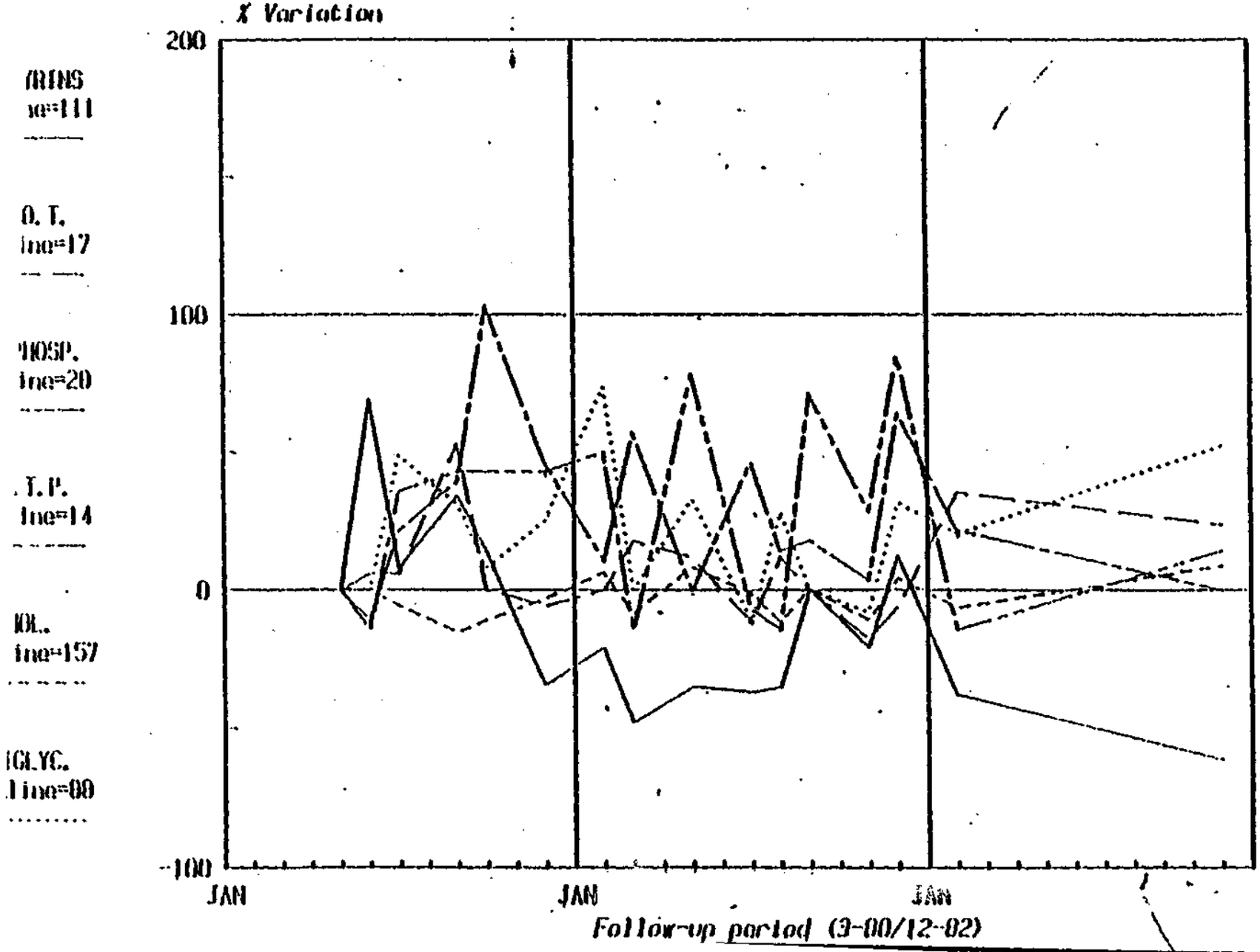


Fig.45 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #8: S.R., 49 yrs

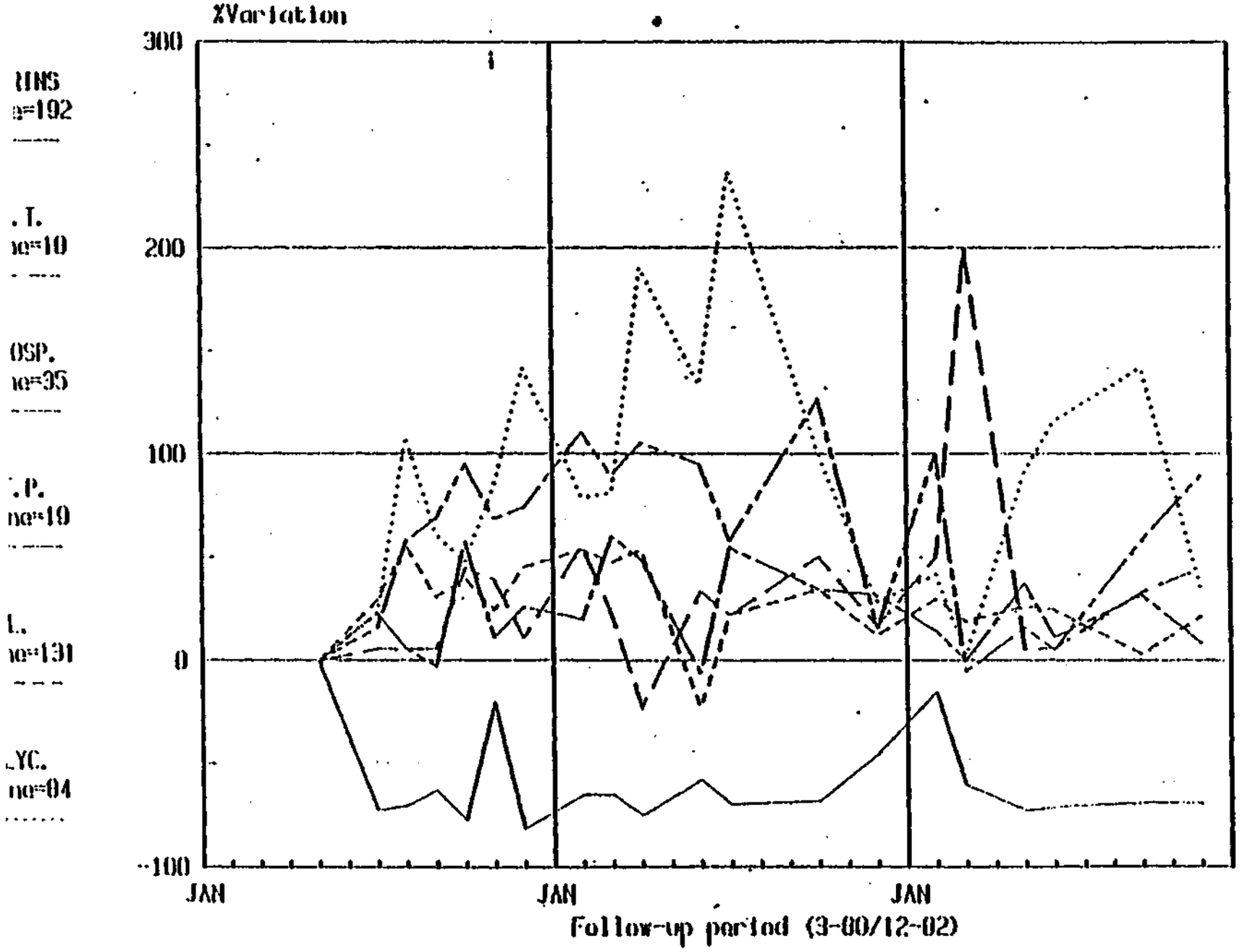


Fig. 46 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #9: C. Z., 29 yrs.

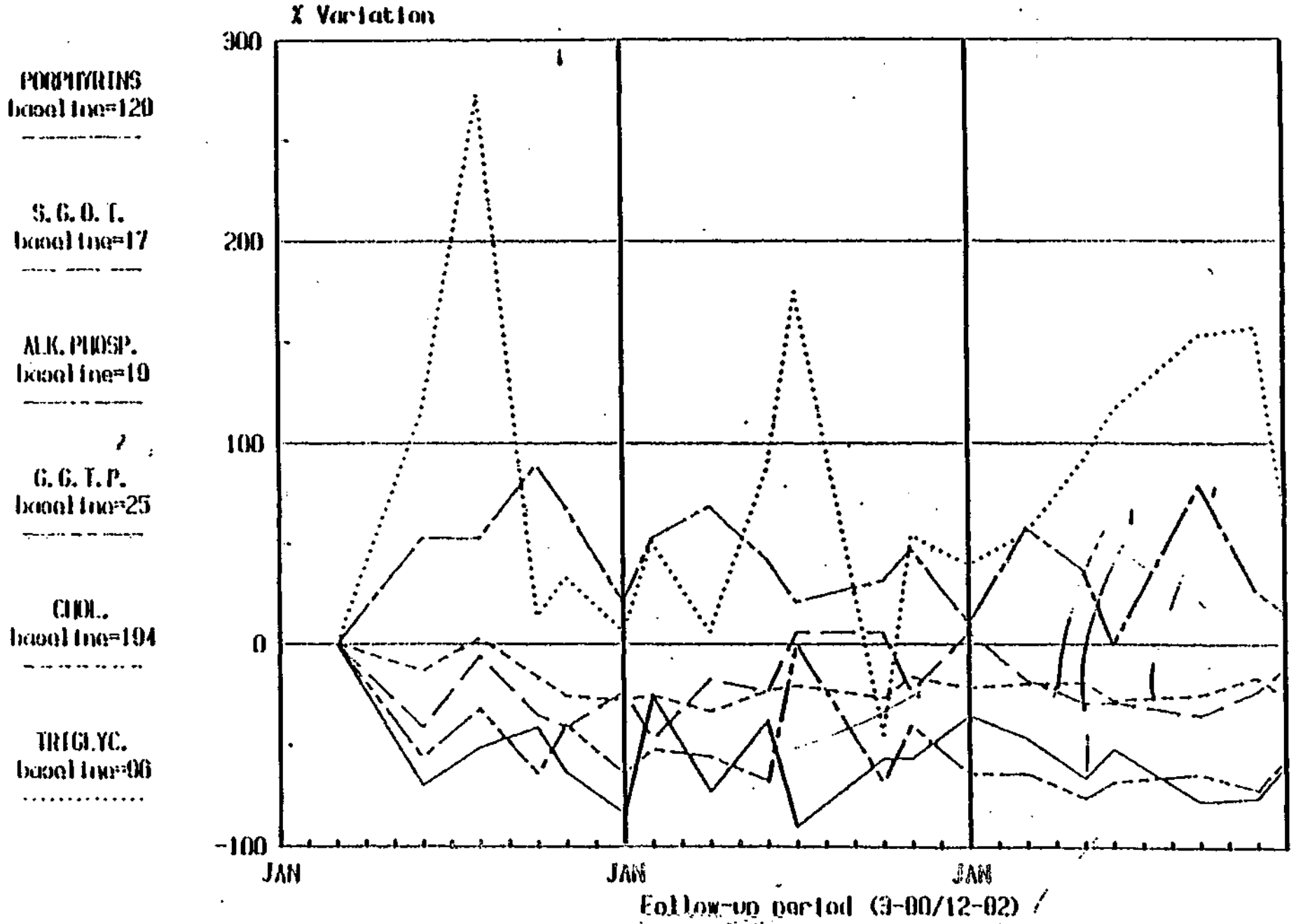


Fig.47 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #10: F.L., 39 yrs.

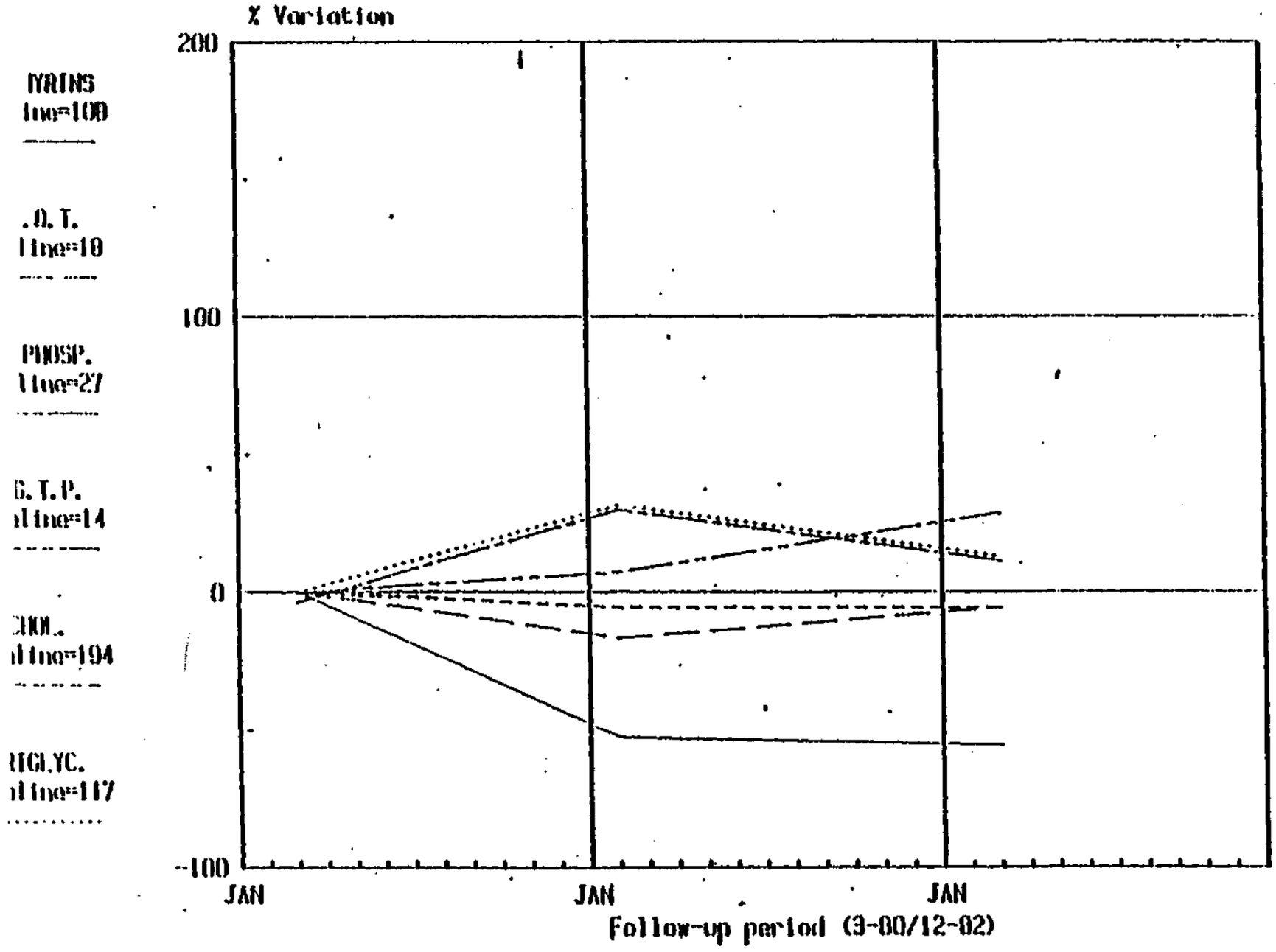


Fig. 48 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #11: L. A., 30 yrs.

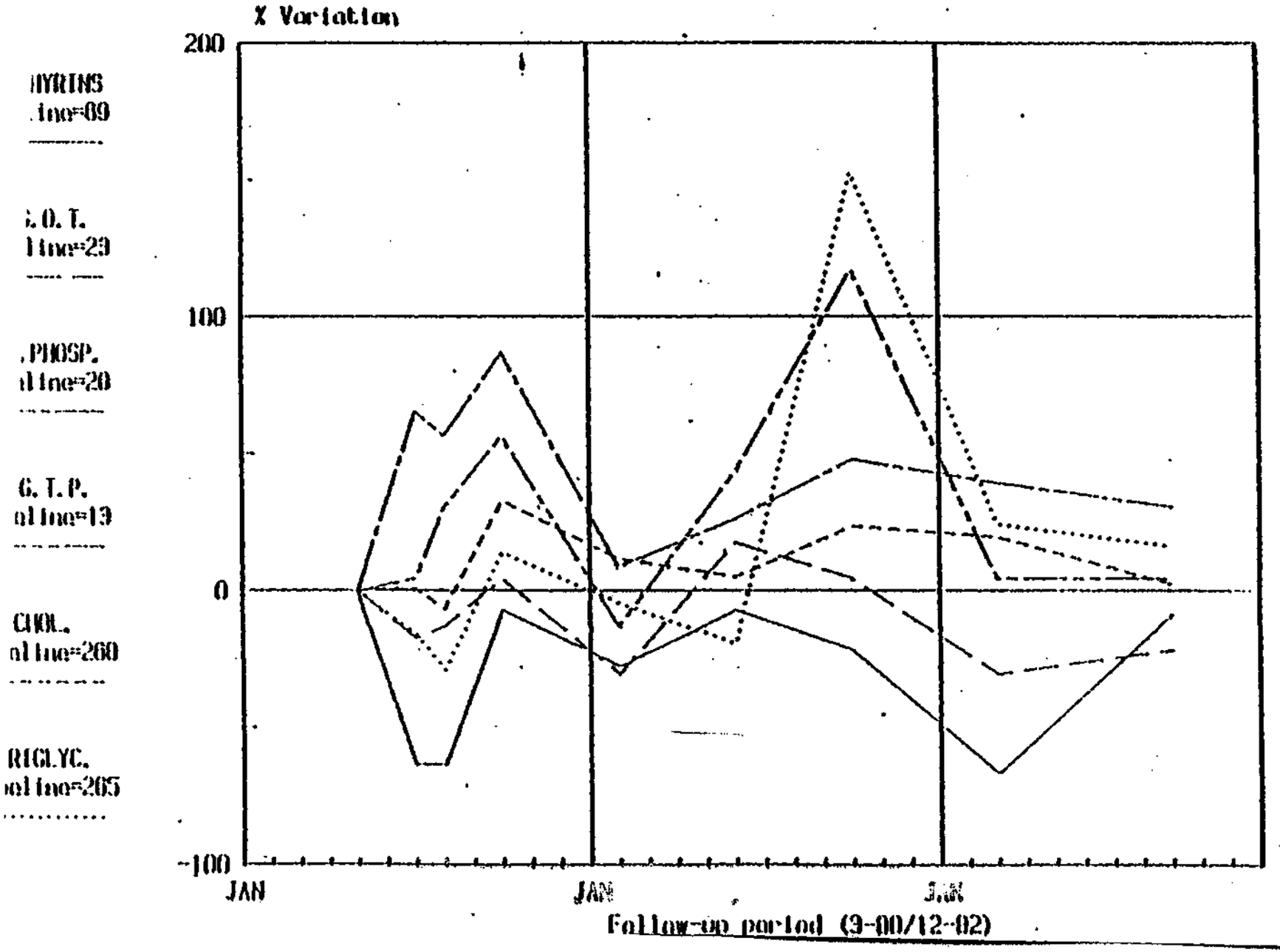


Fig. 49 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #12: M.R., 24 yrs.

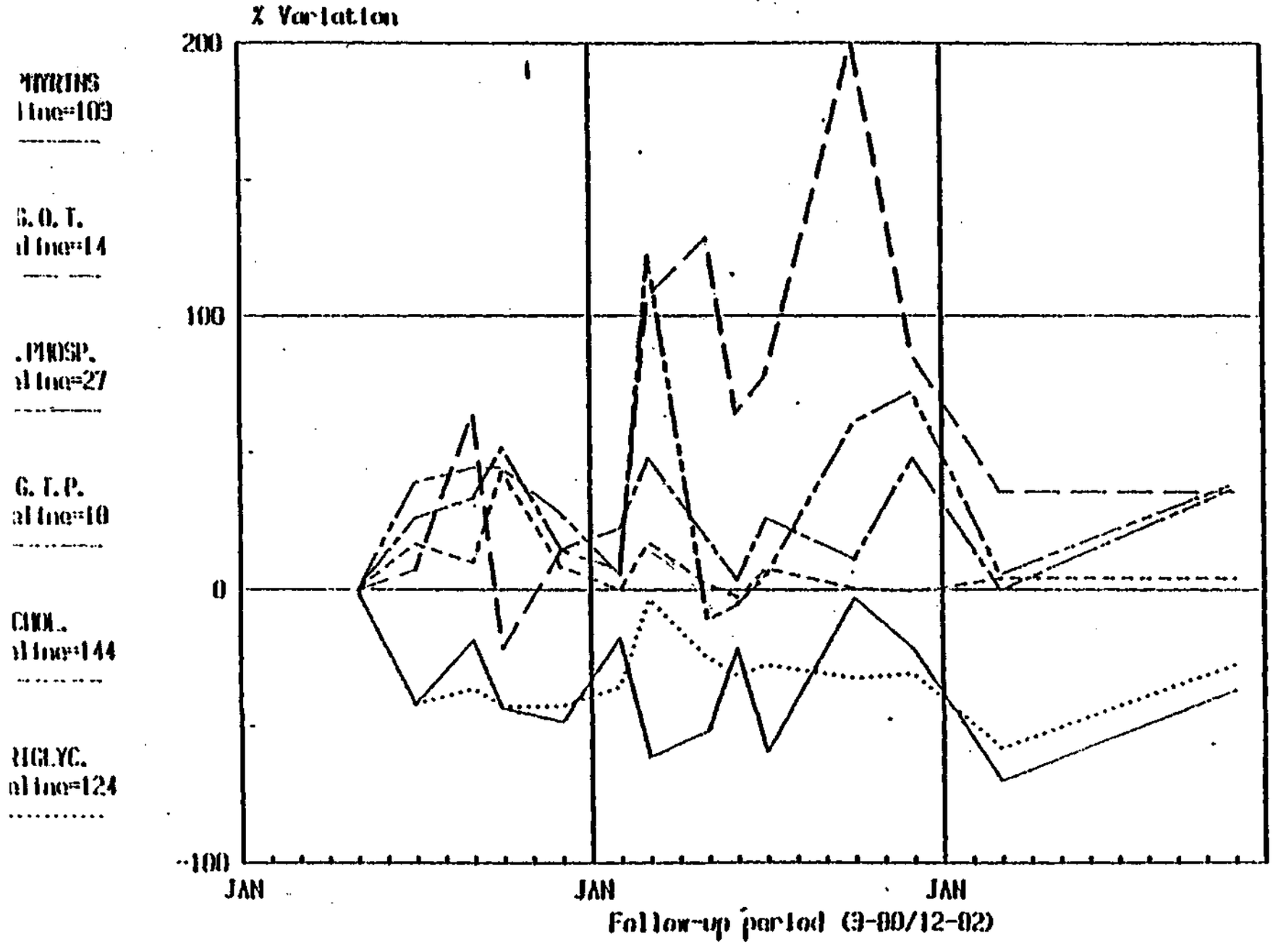


Fig. 50 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #13; A.F., 46 yrs.

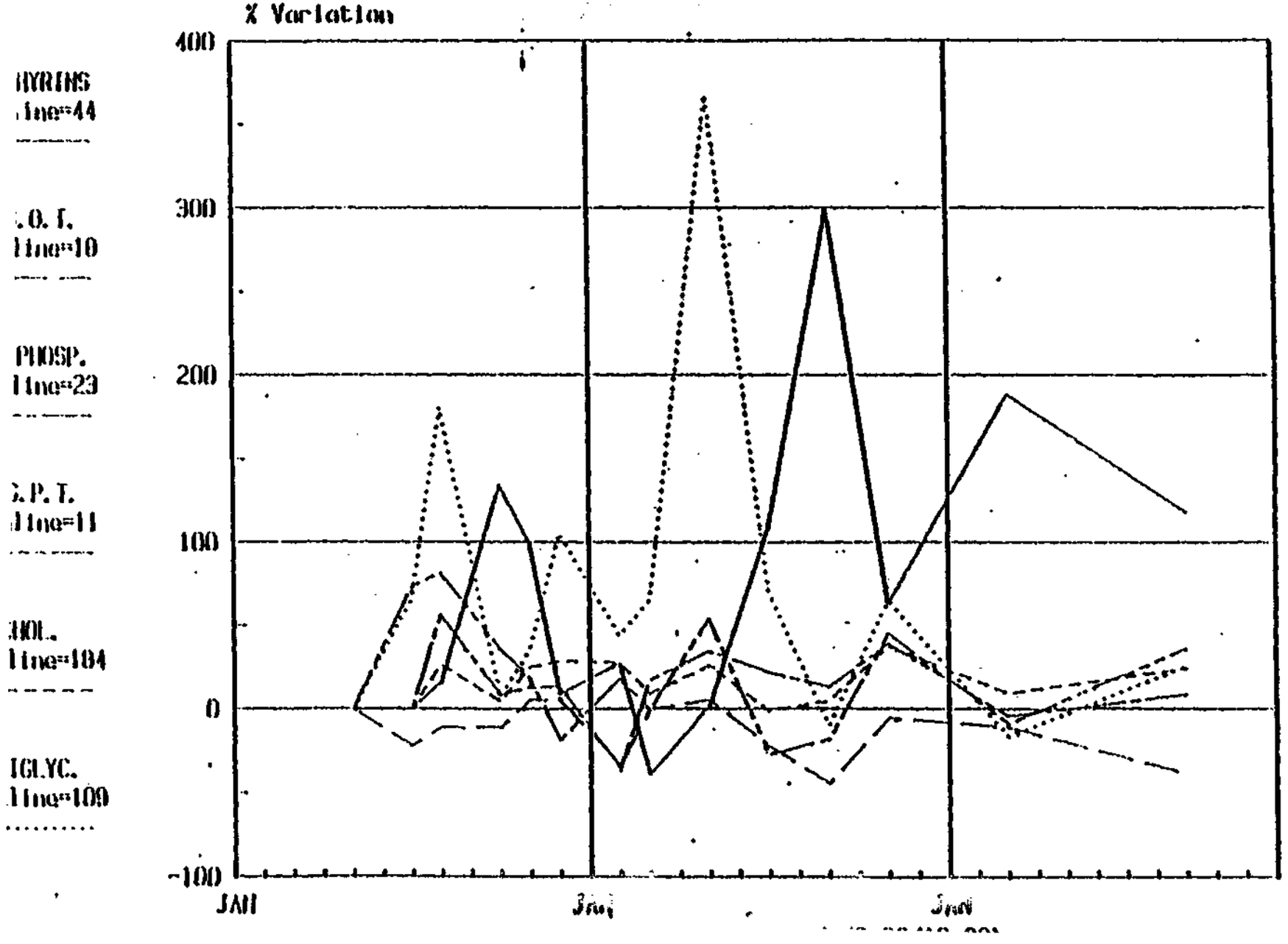


Fig.51 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #14: G. C., 44 yrs.

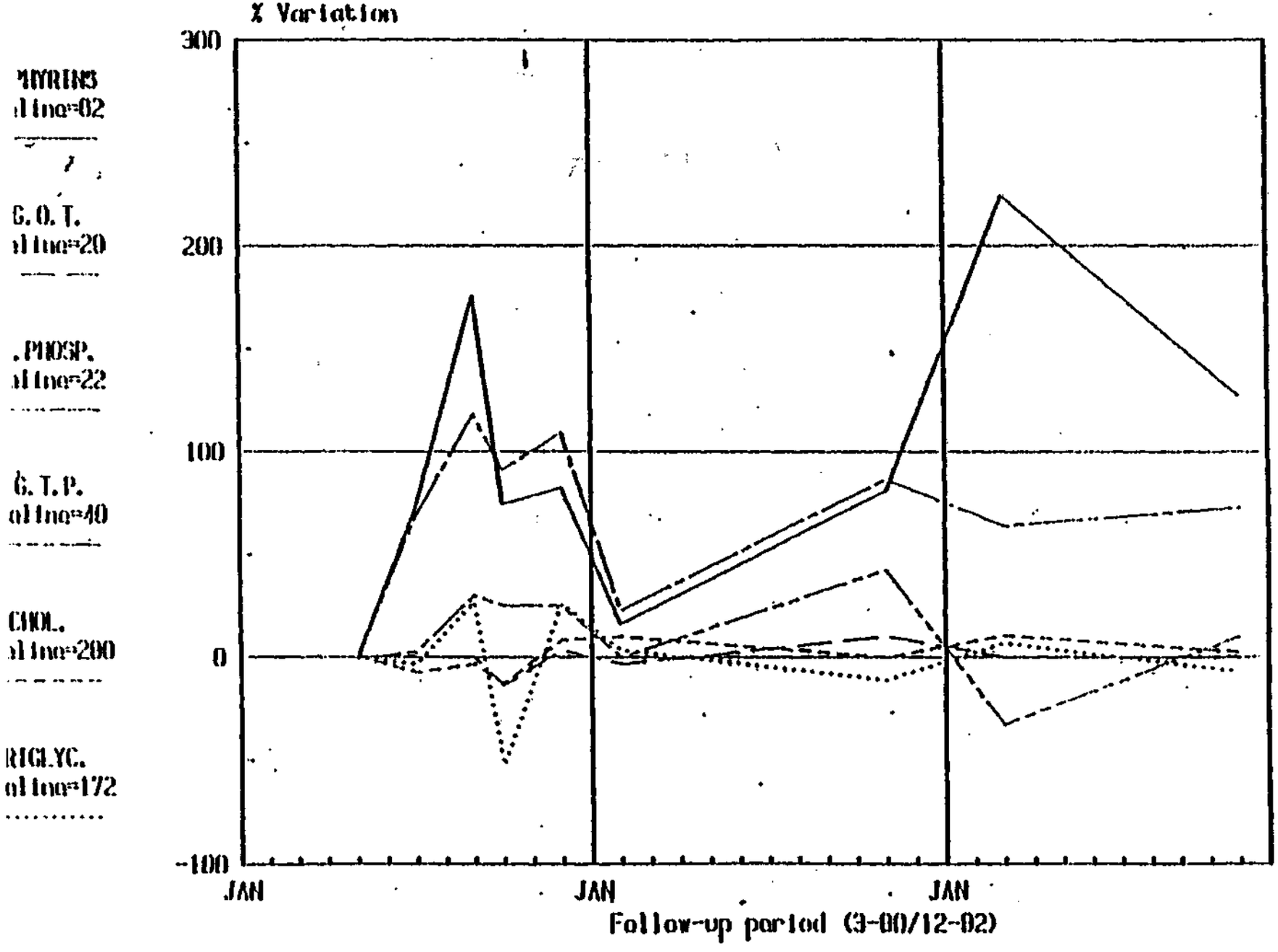


Fig. 52 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #15; S, C., 24 yrs.

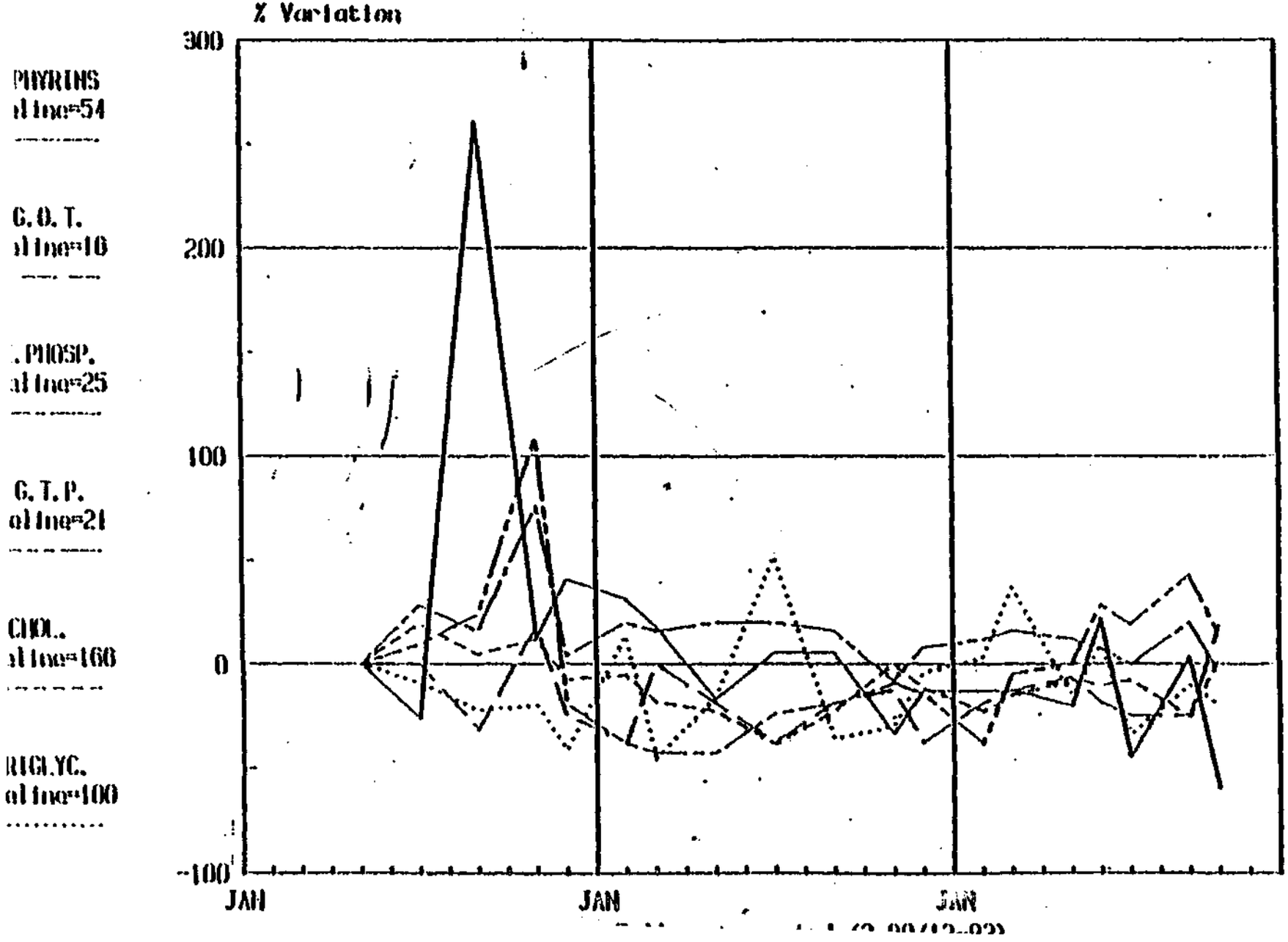


Fig. 53 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #16: E.P., 30 yrs.

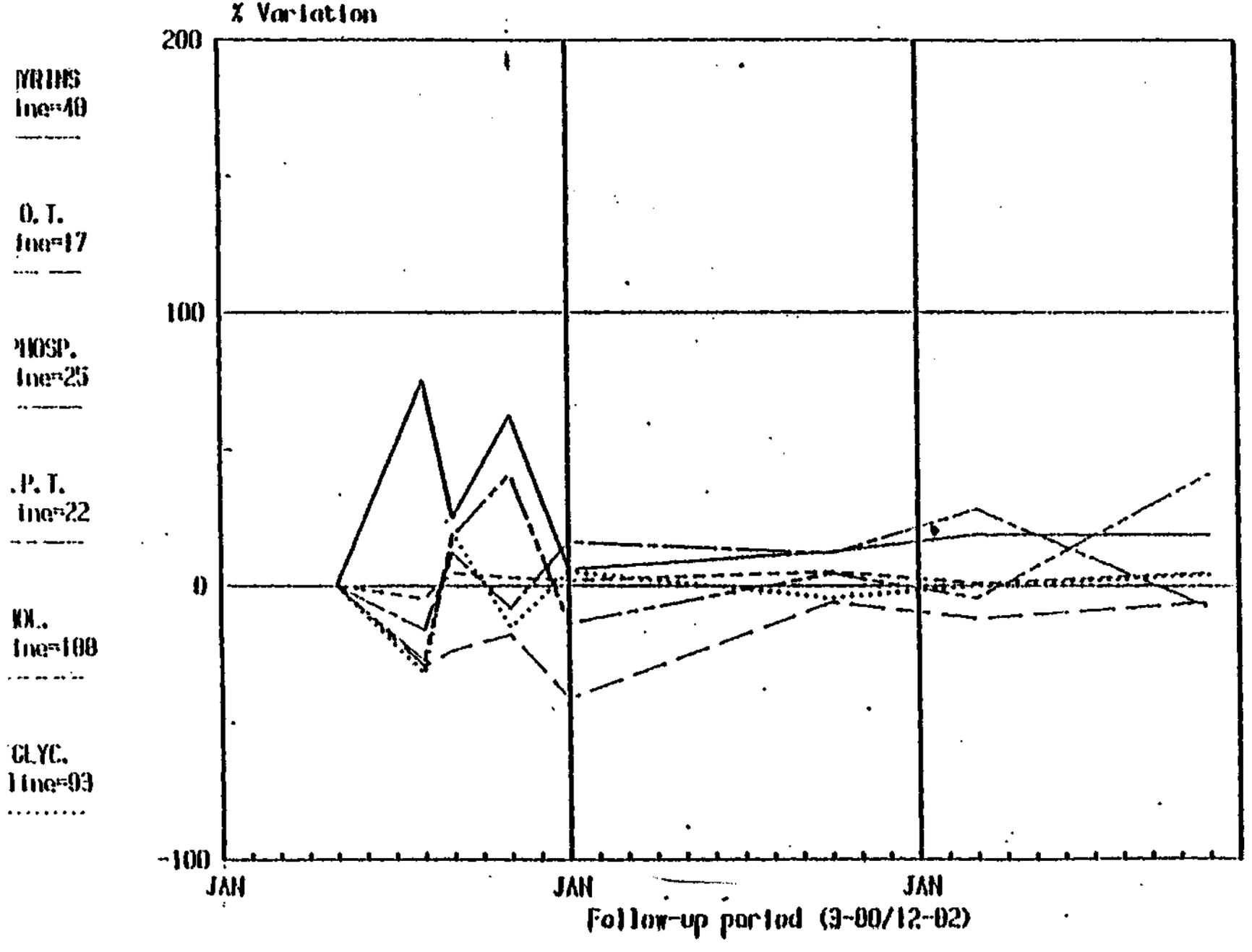


Fig. 54 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #17: G.R., 35 yrs.

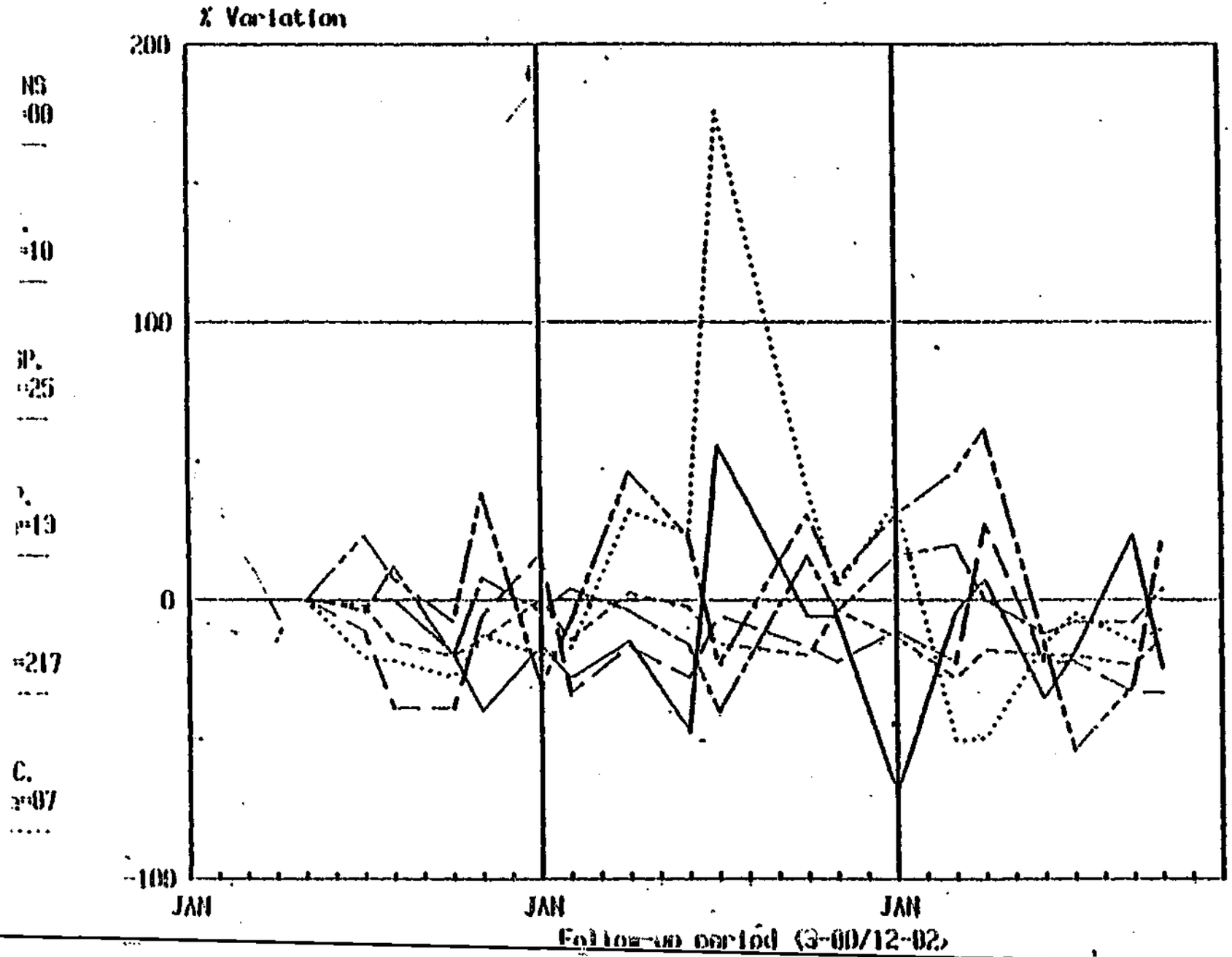


Fig.55. TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #18: A.C., 34 yrs.

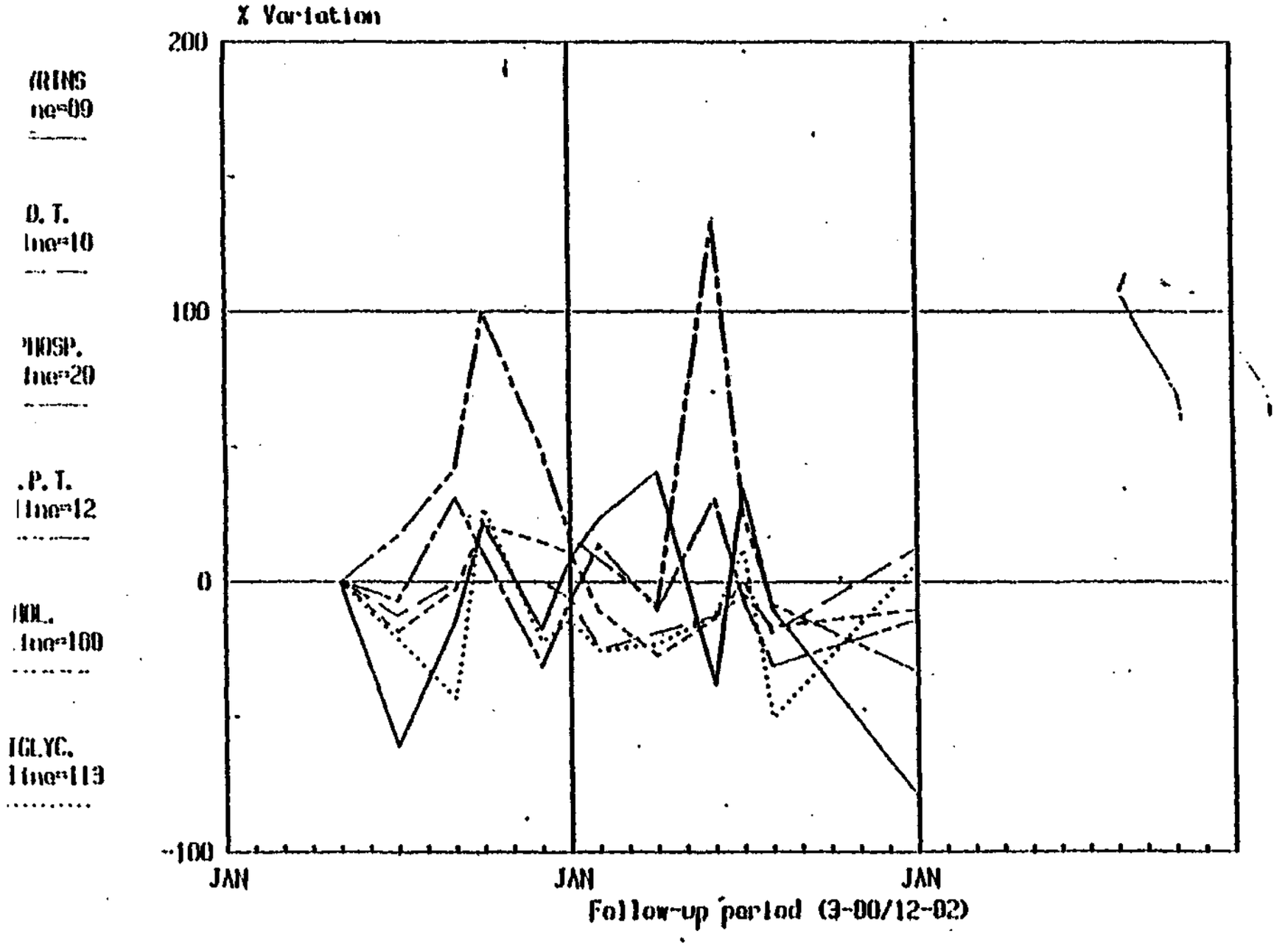


Fig. 56 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #19: S. C., 23 yrs.

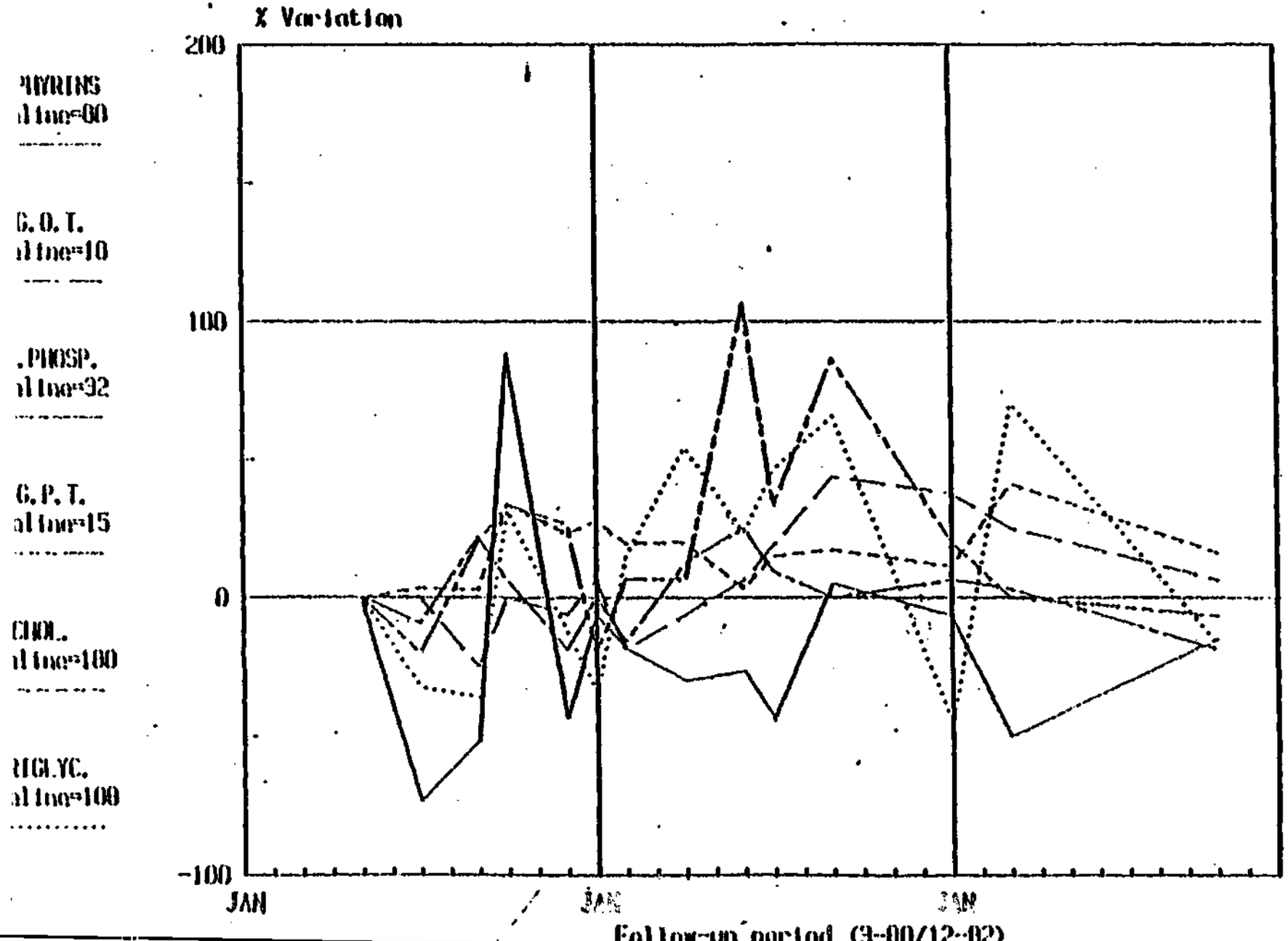


Fig. 57 TIME TRENDS OF 6 PARAMETERS in CLEAN-UP WORKER #20: W.R., 43 yrs.

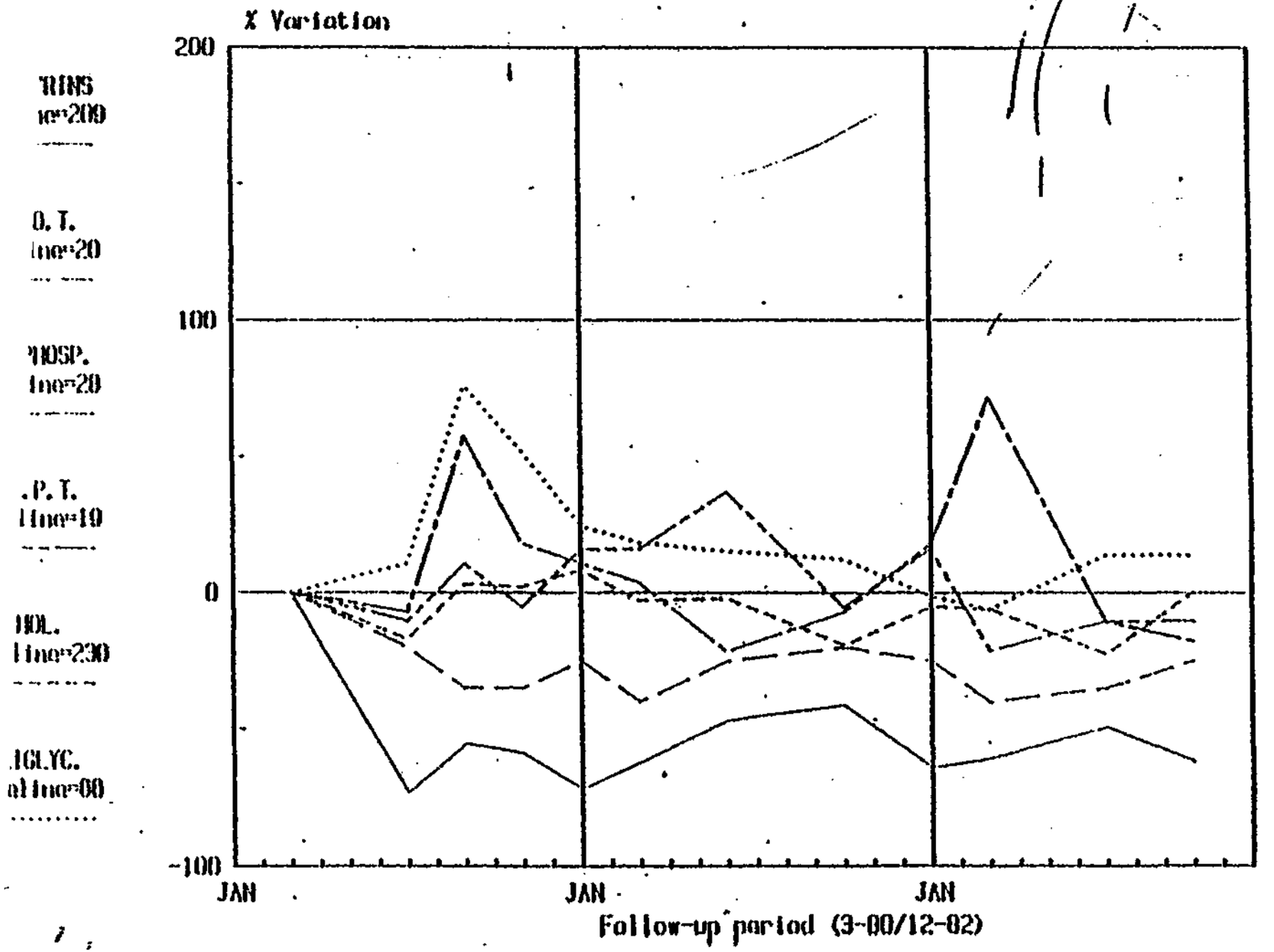


Fig. 58 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #21: G. I., 45 yrs.

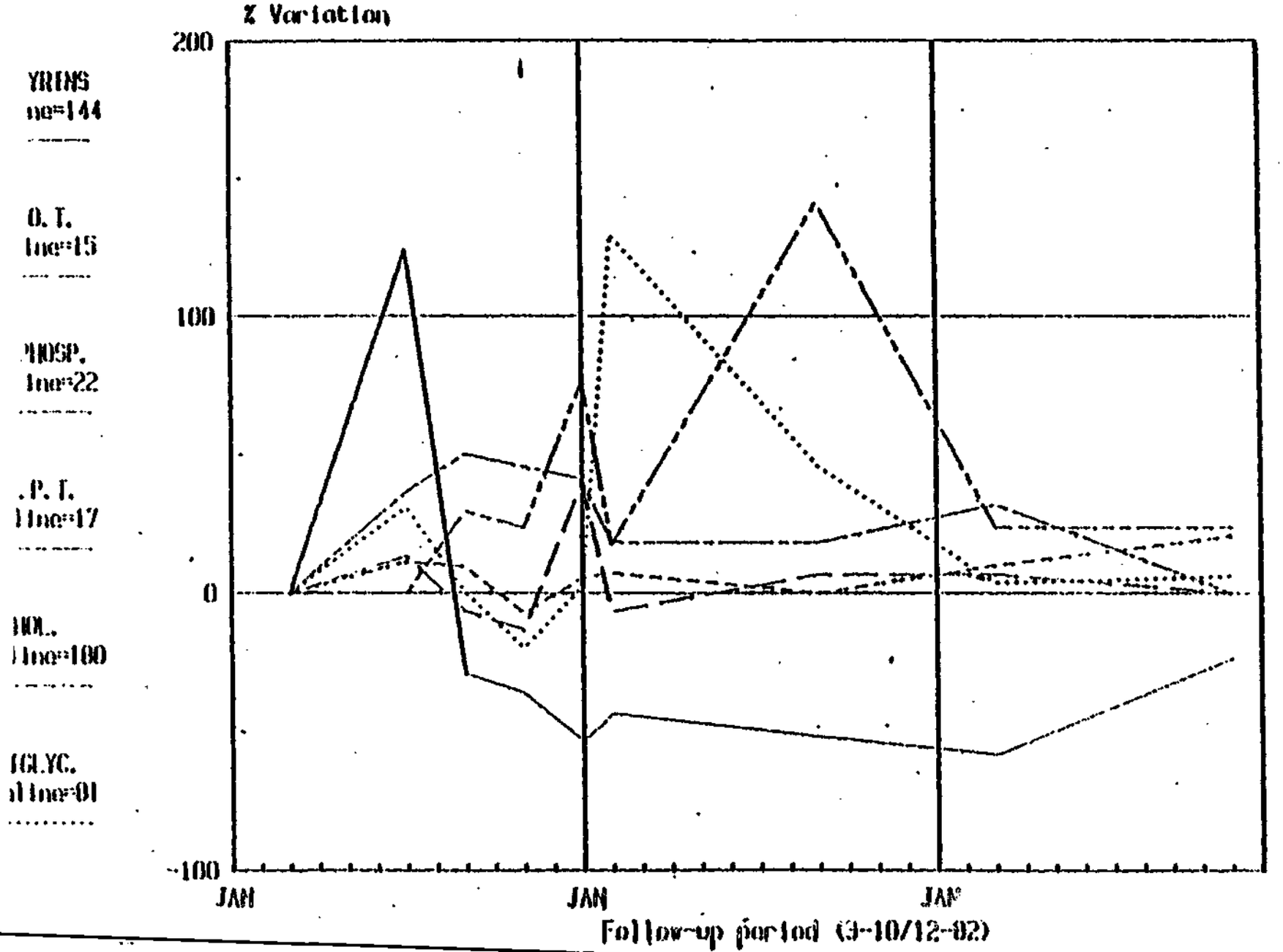


Fig. 59 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #22: E.B., 35 yrs.

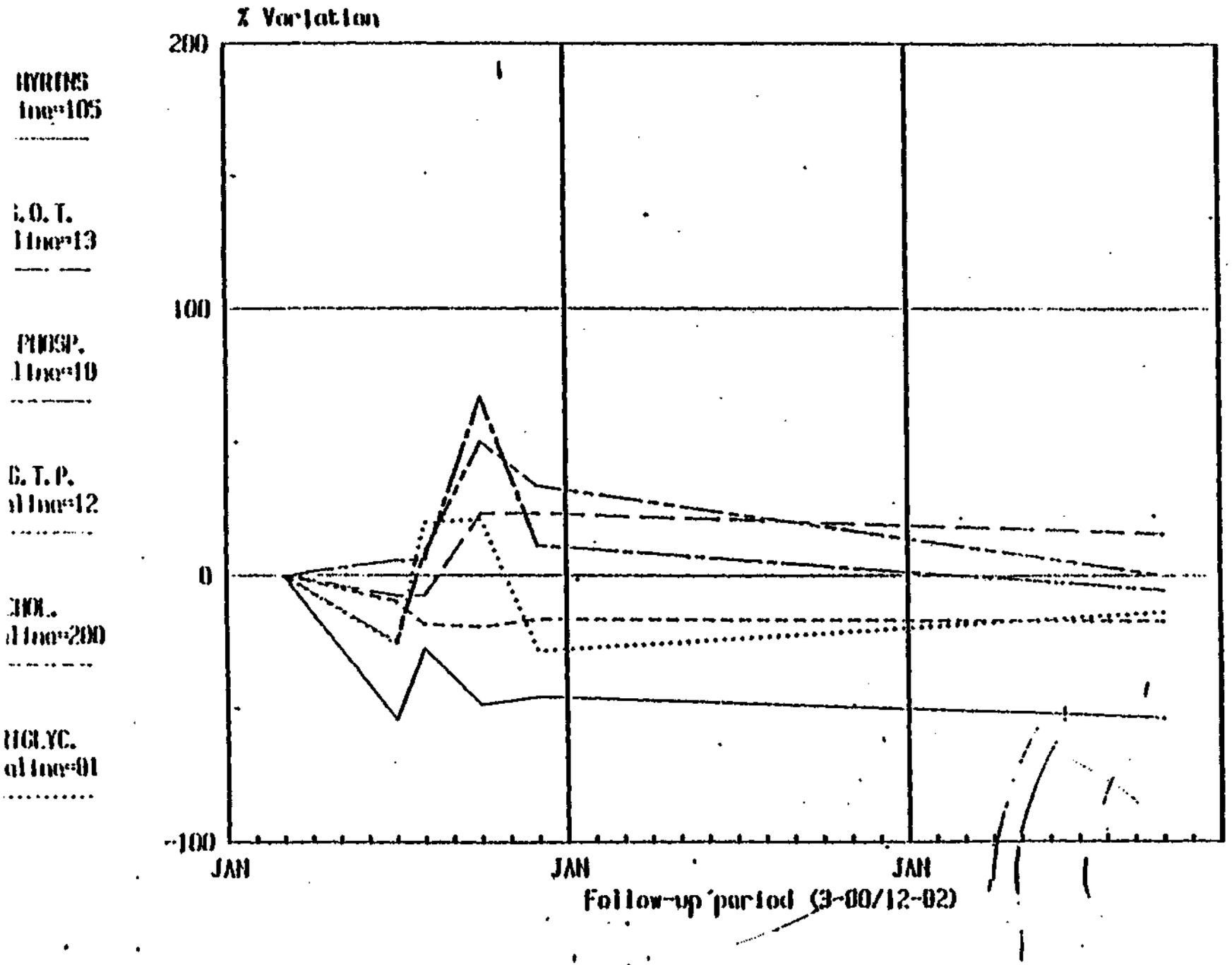


Fig. 60 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #23: F. C., 46 yrs.

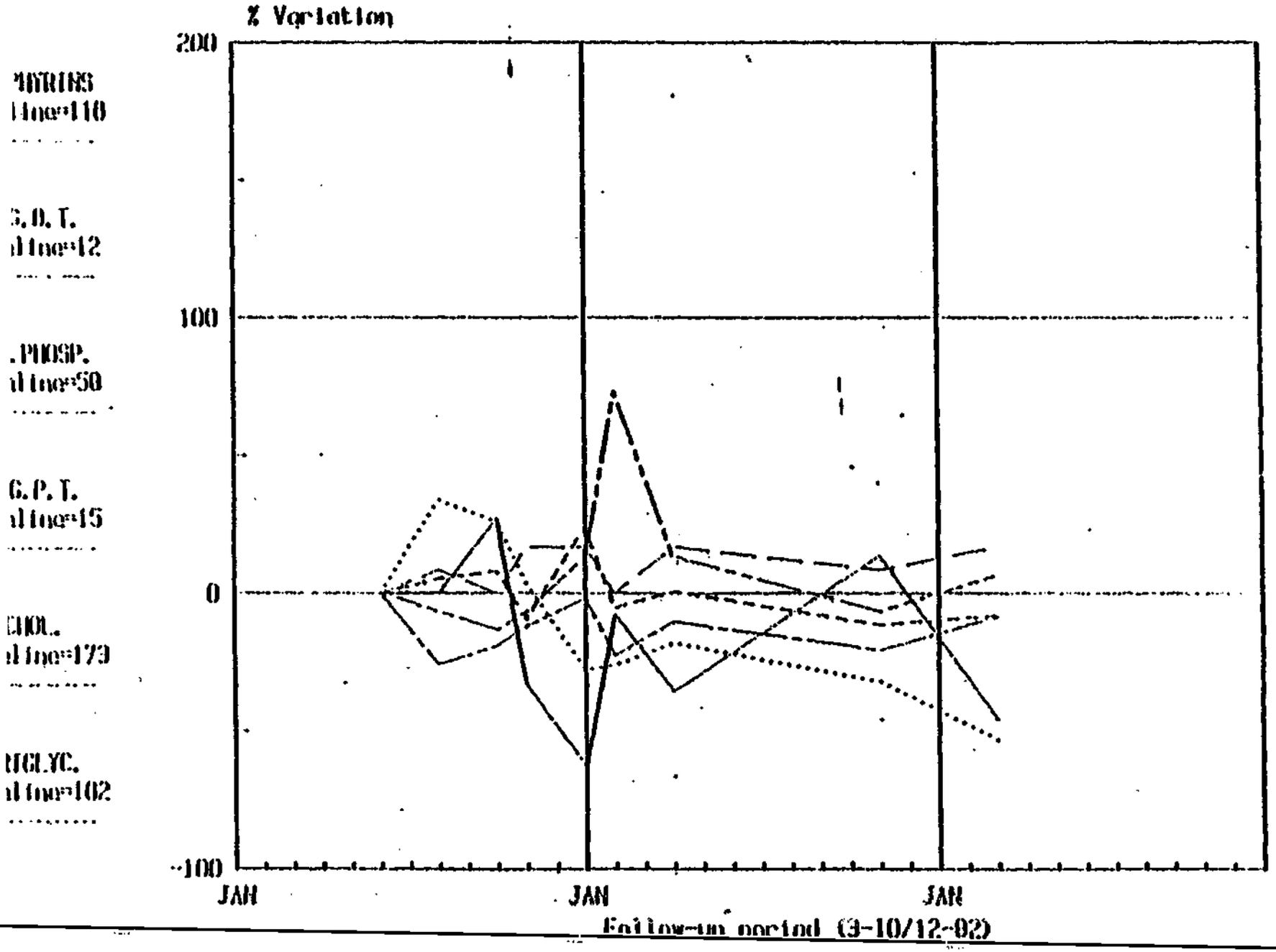


Fig. 61 TIME TRENDS [illegible]

CLEAN-UP WORKER #24: M. V., 34 yrs.

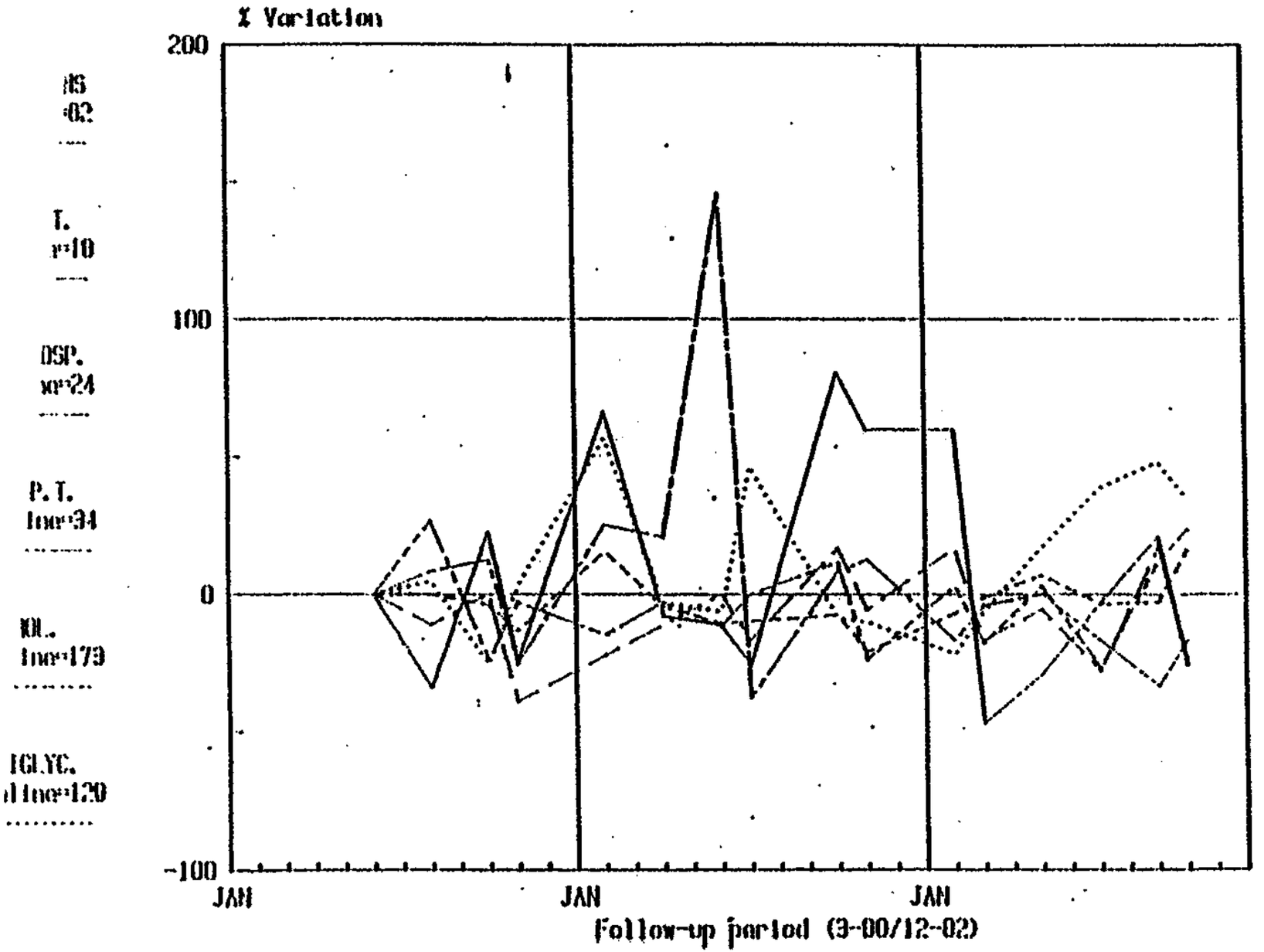


Fig. 62 TIME TRENDS OF 6 PARAMETERS IN
CLEAN-UP WORKER #25: A.S., 51 yrs

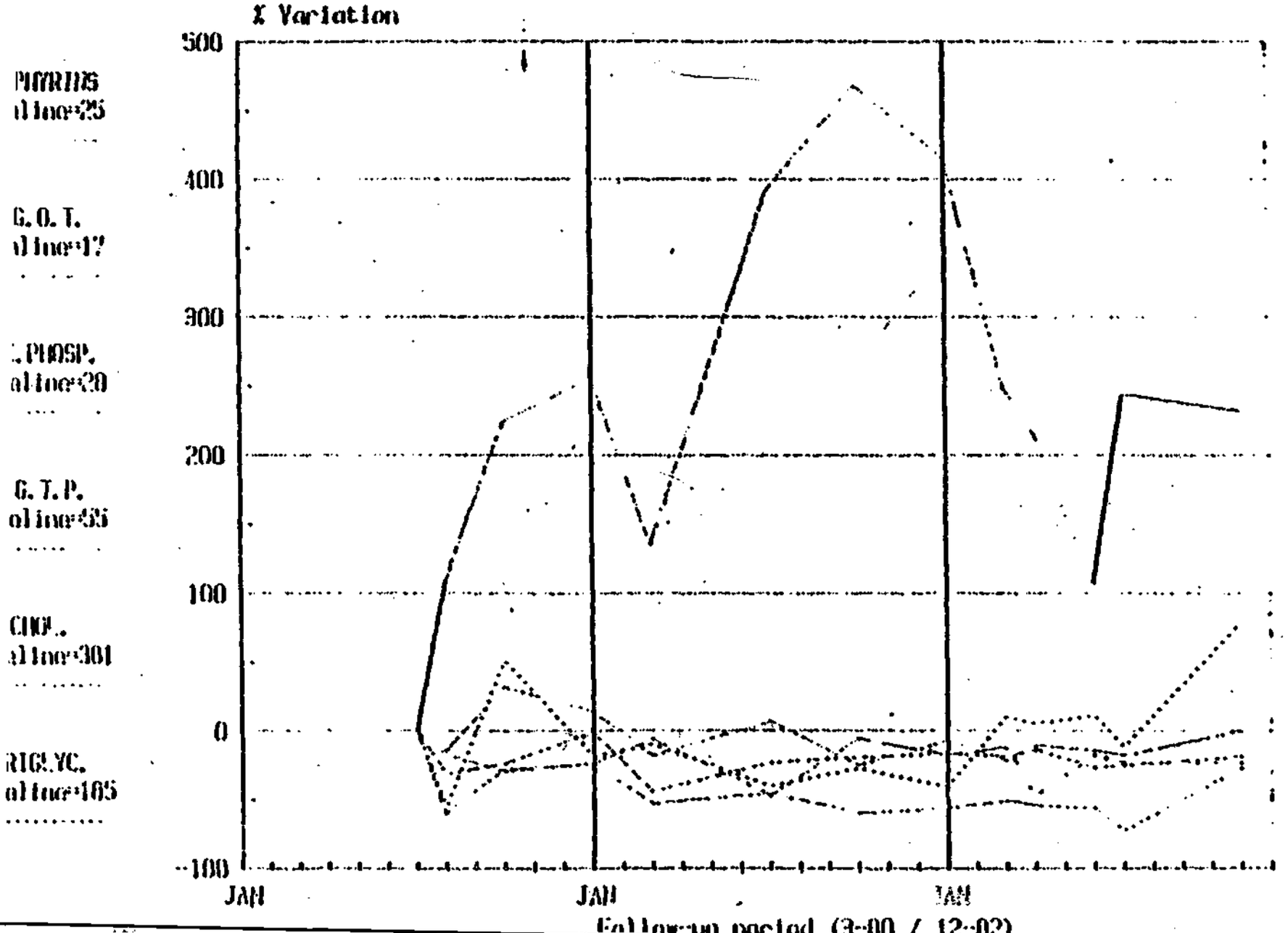


Fig.63 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #26: A.G., 24 yrs

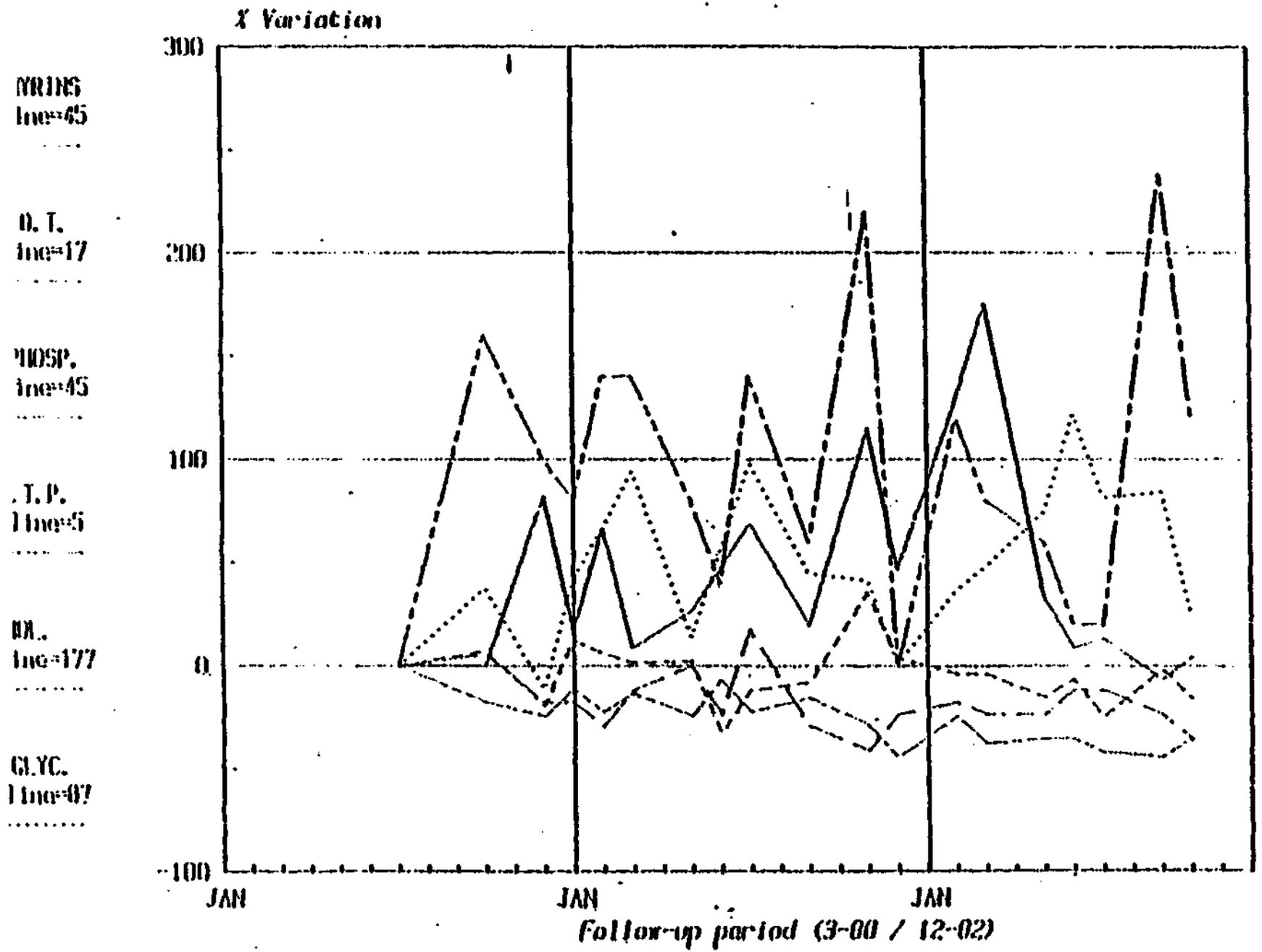


Fig. 64 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #27: H.S., 30 yrs

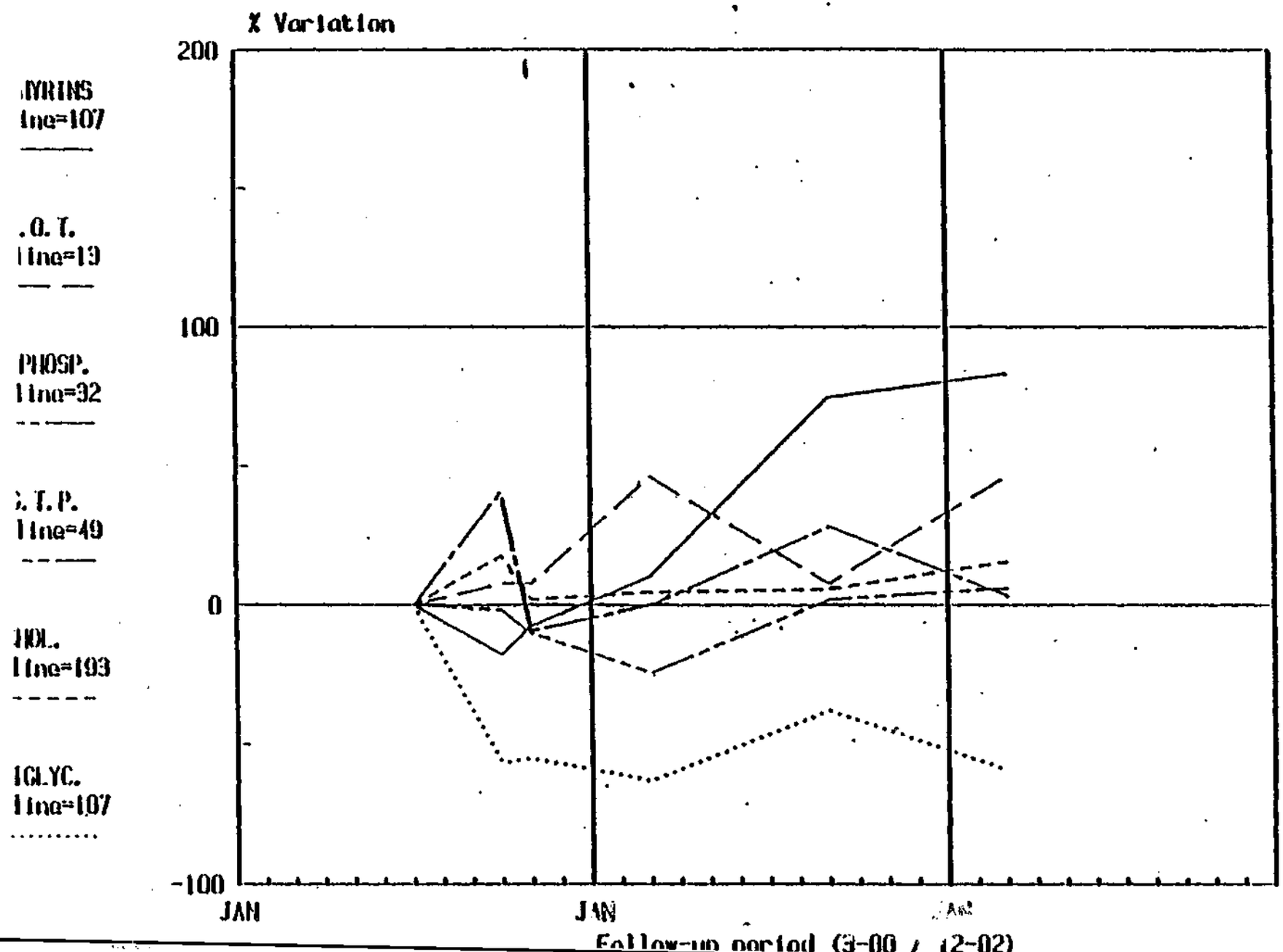


Fig. 65 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #28: J.S., 36 yrs

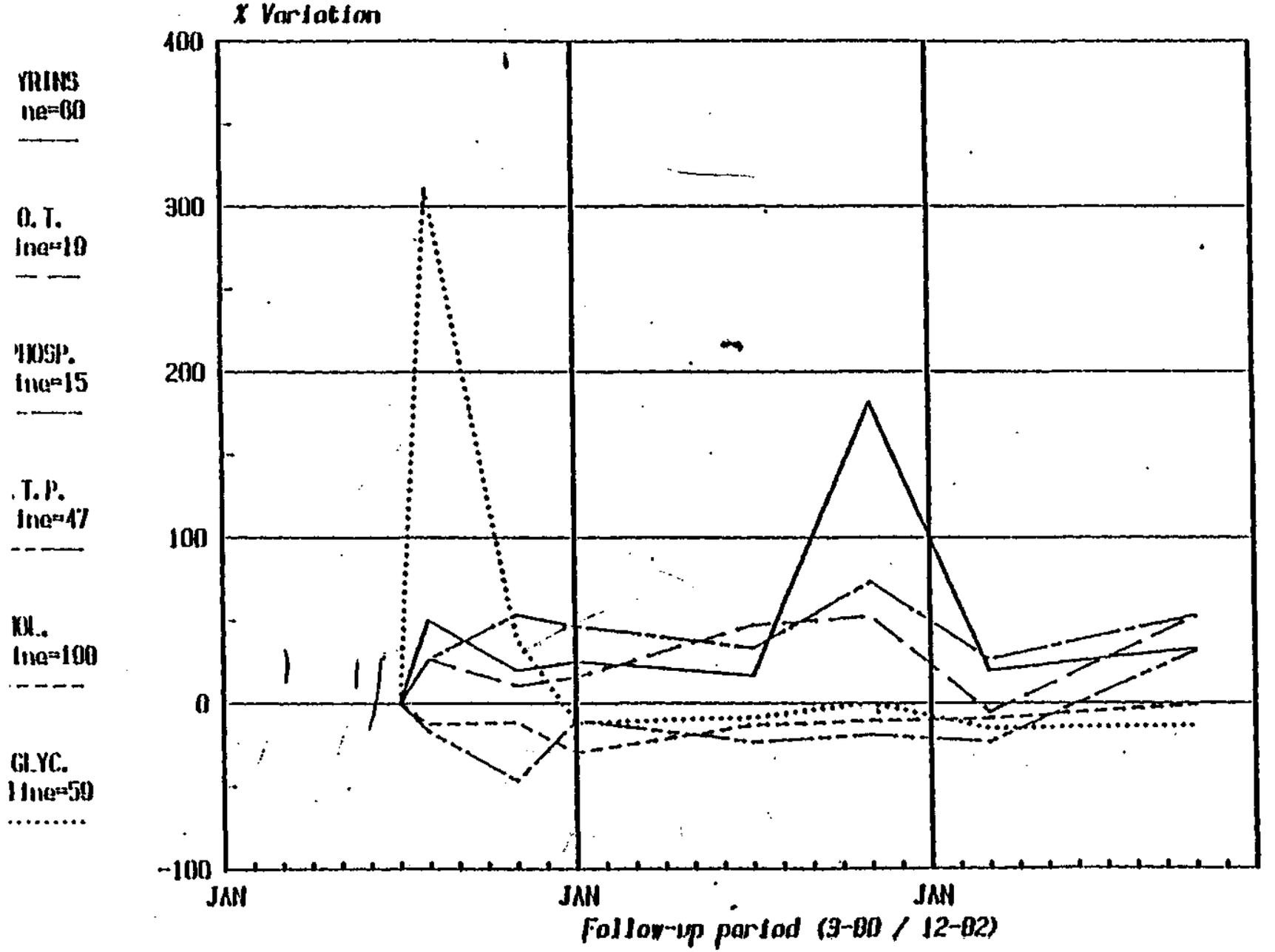


Fig. 66 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #29: G.F., 43 yrs

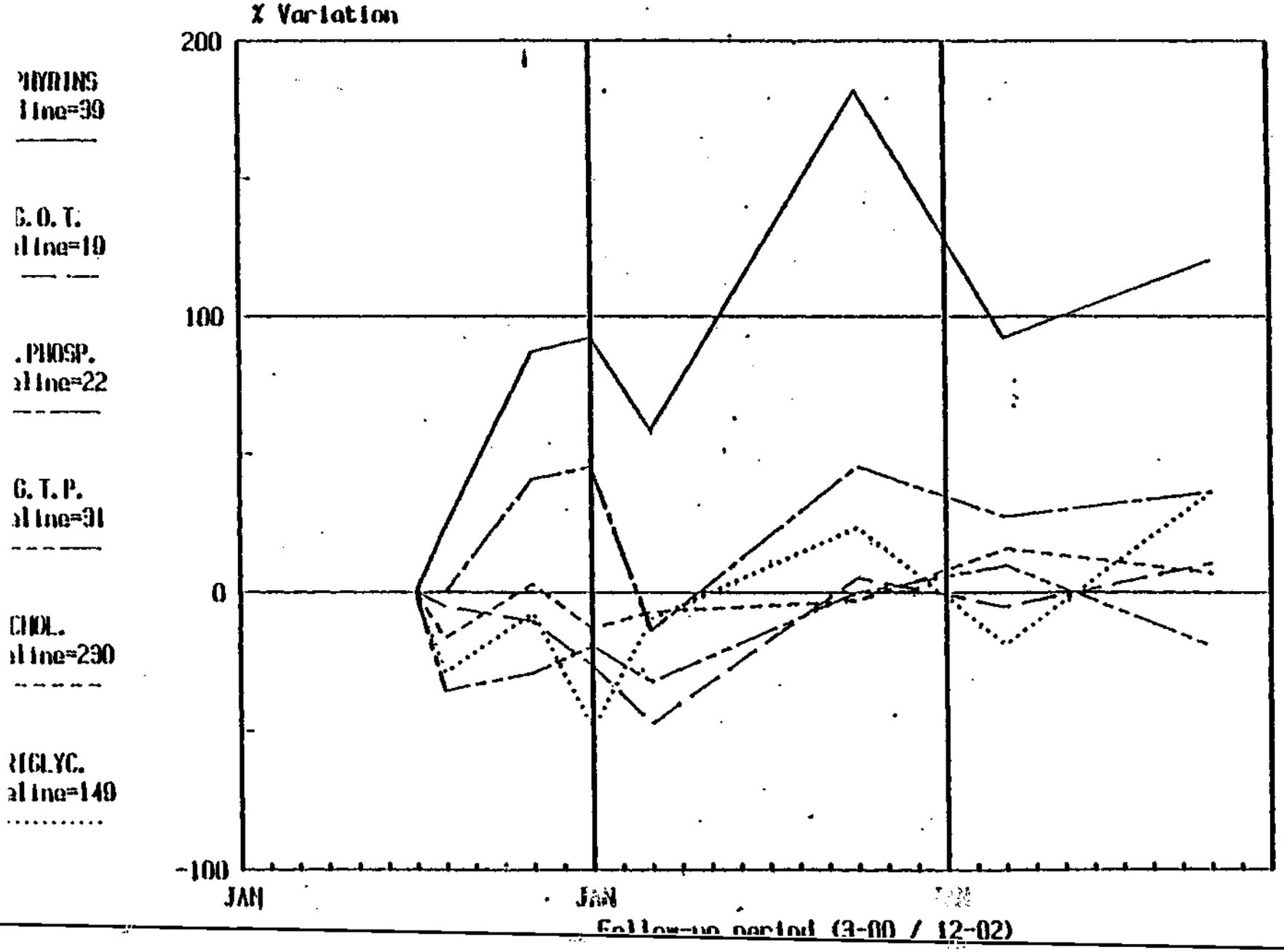


Fig.67 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #30: R.R., 23 yrs

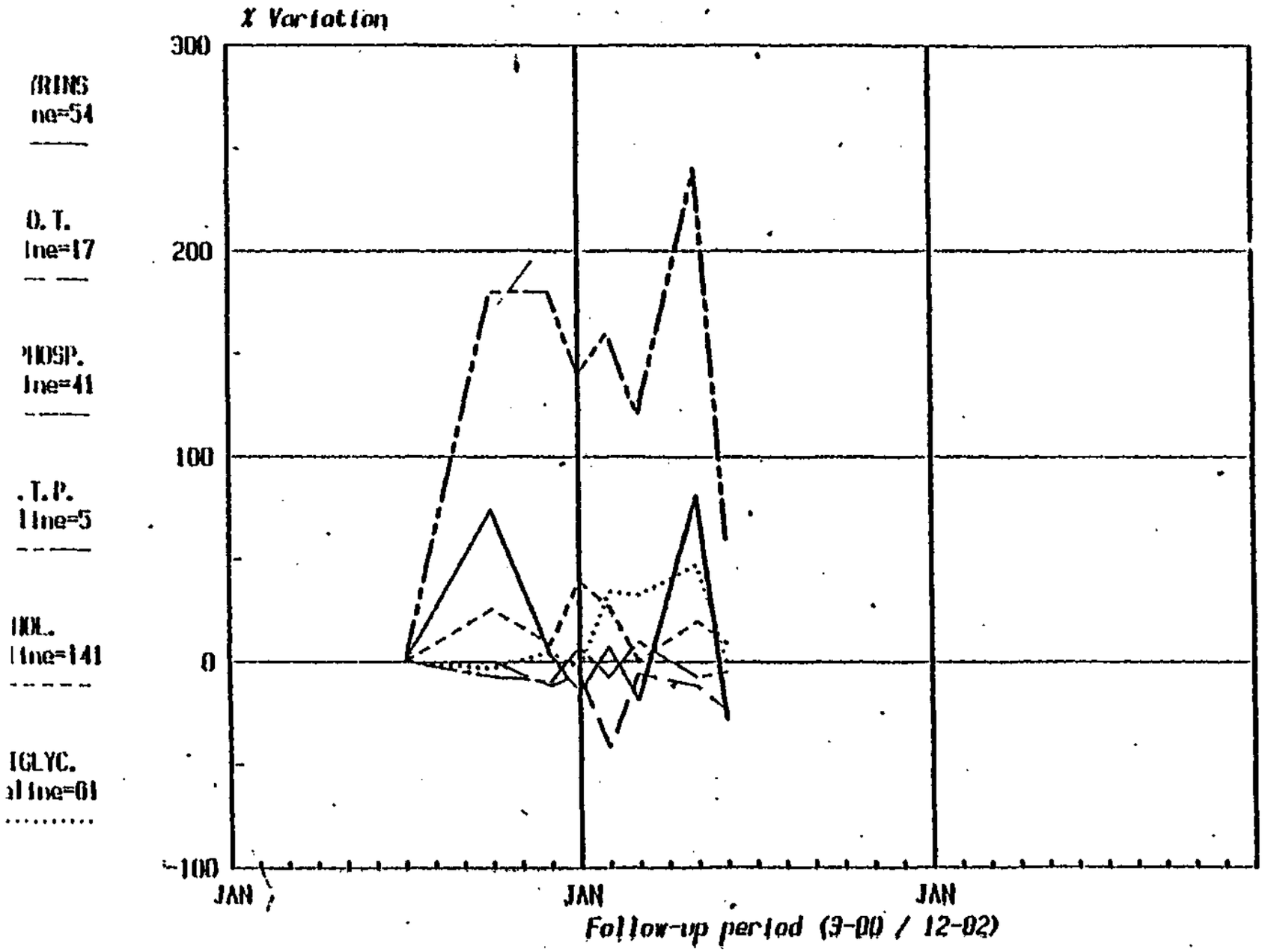


Fig. 68 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #31: N.F., 37 yrs

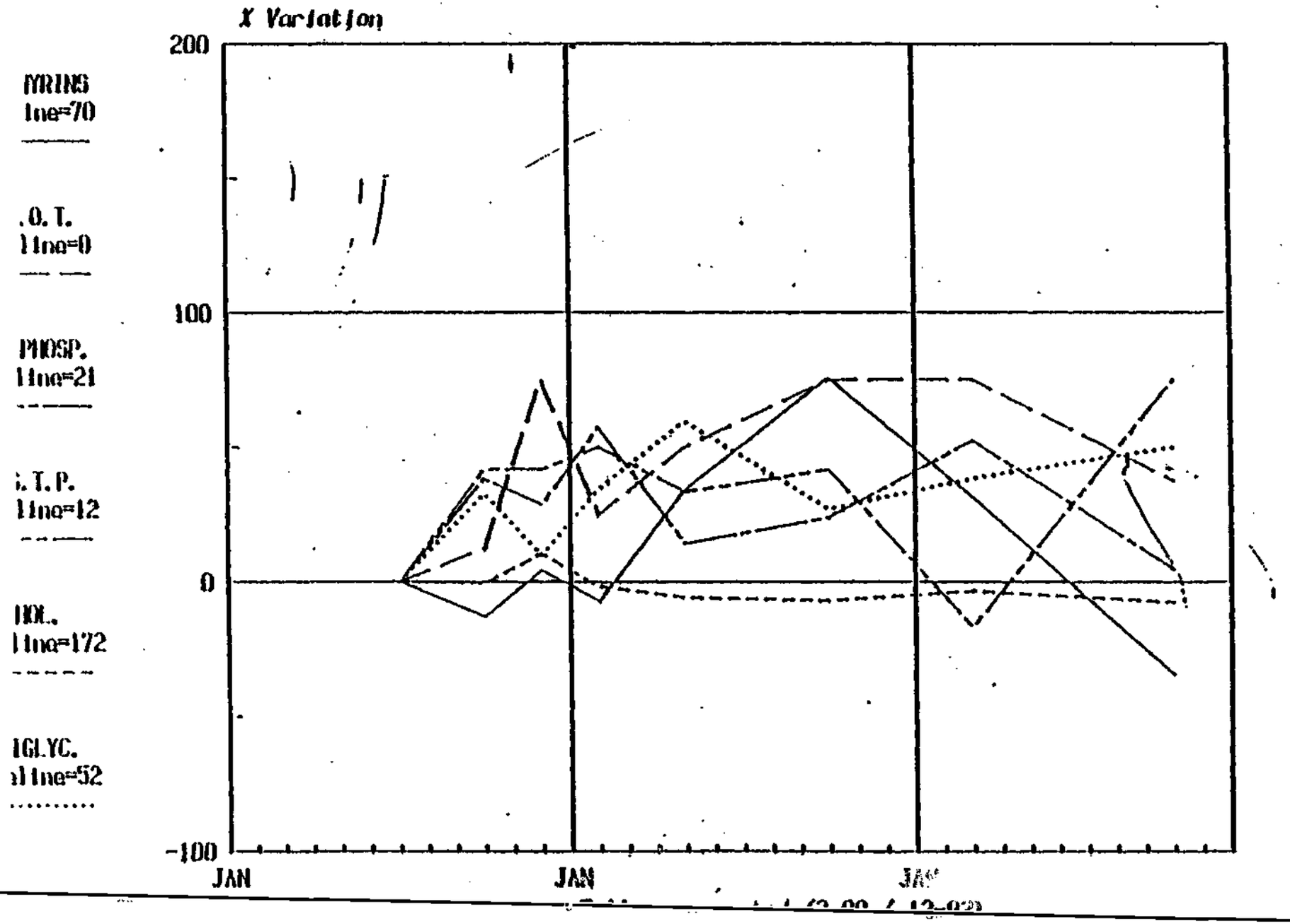


Fig.69 TIME TRENDS OF [illegible]

CLEAN-UP WORKER #32: F.D., 27 yrs

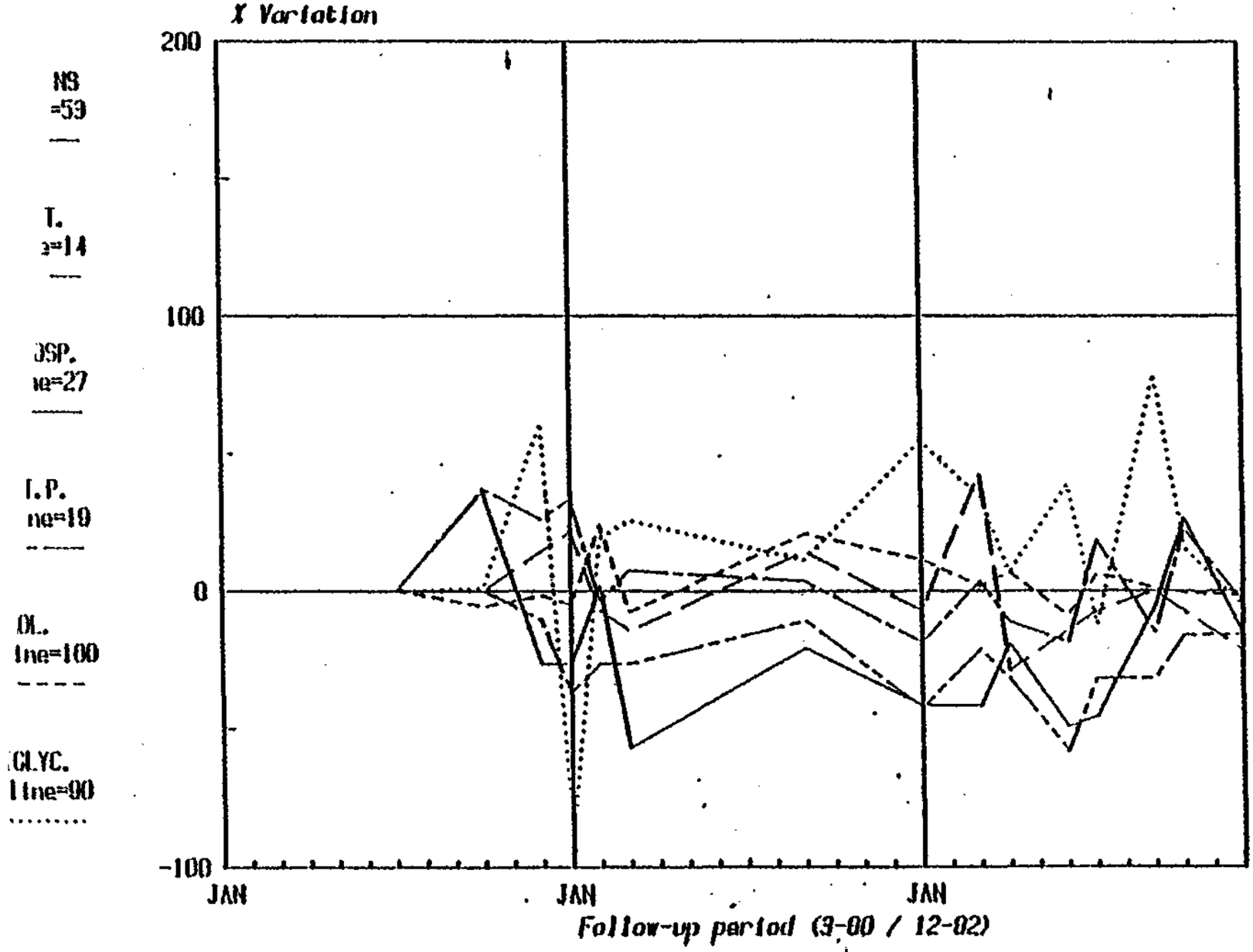


Fig.70 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #33; R.S., 43 yrs

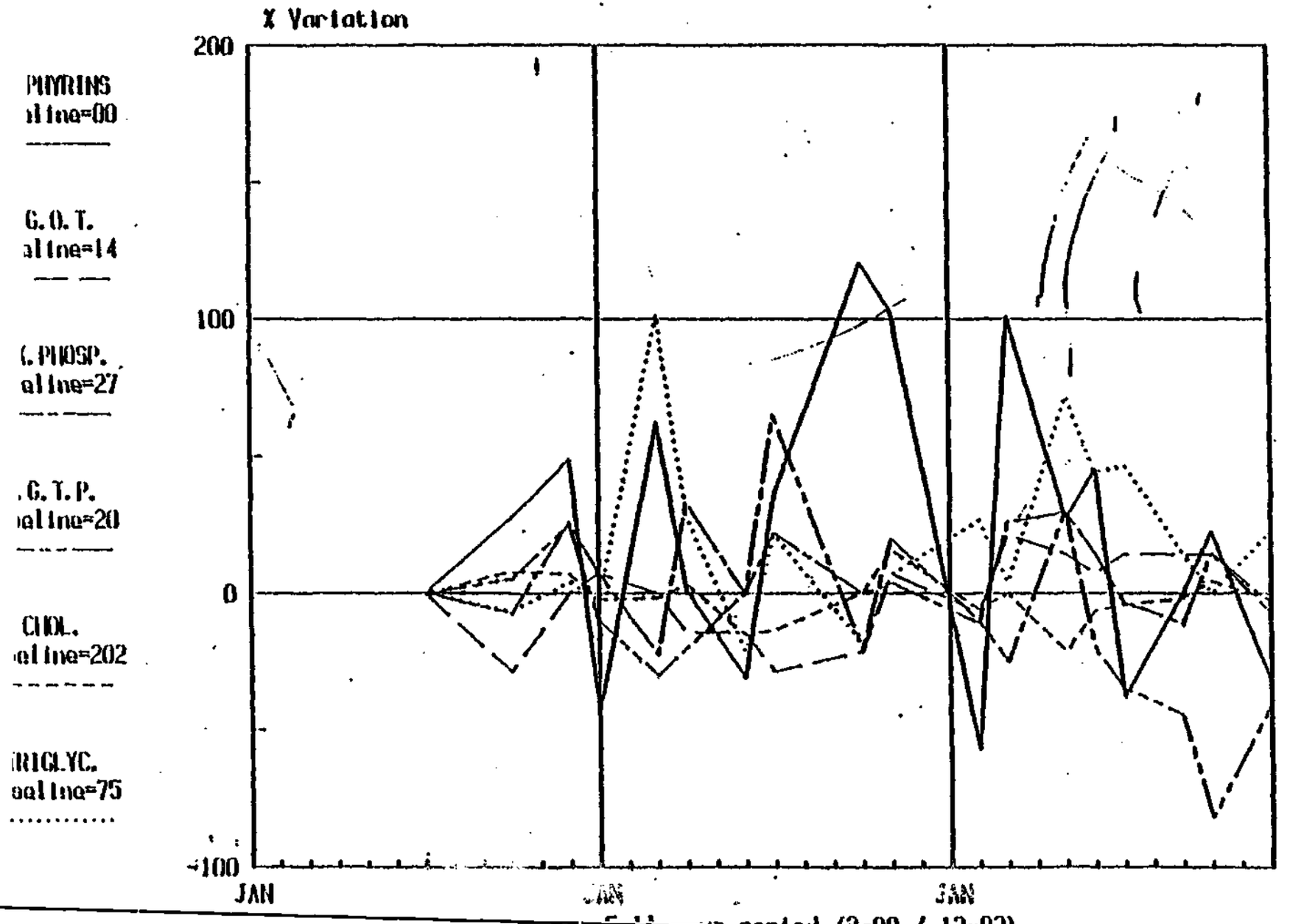


Fig.71 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #34: A.Z., 31 yrs

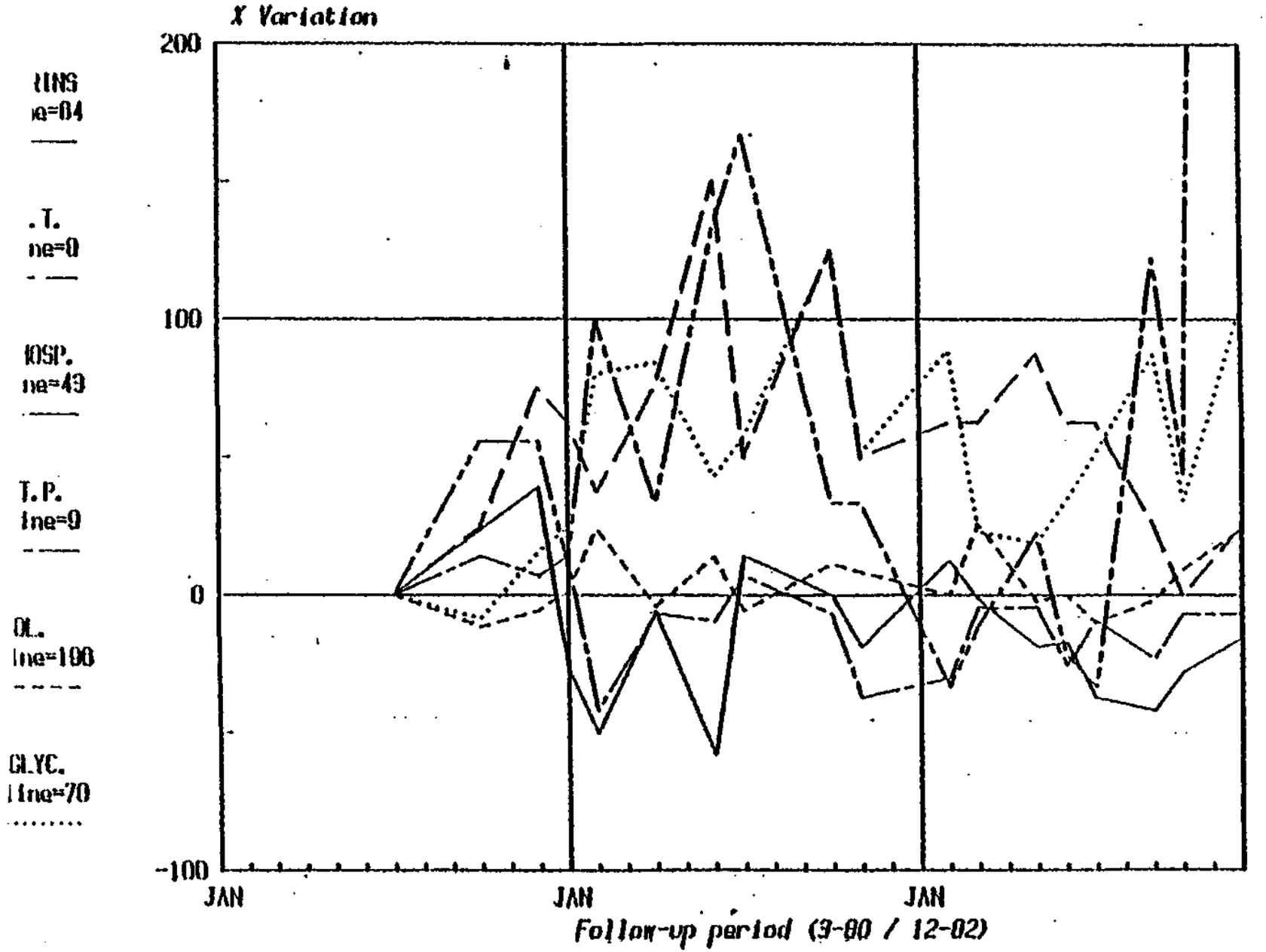


Fig. 72 TIME TRENDS OF 6 PARAMETERS IN
CLEAN-UP WORKER #35: T.C., 33 yrs

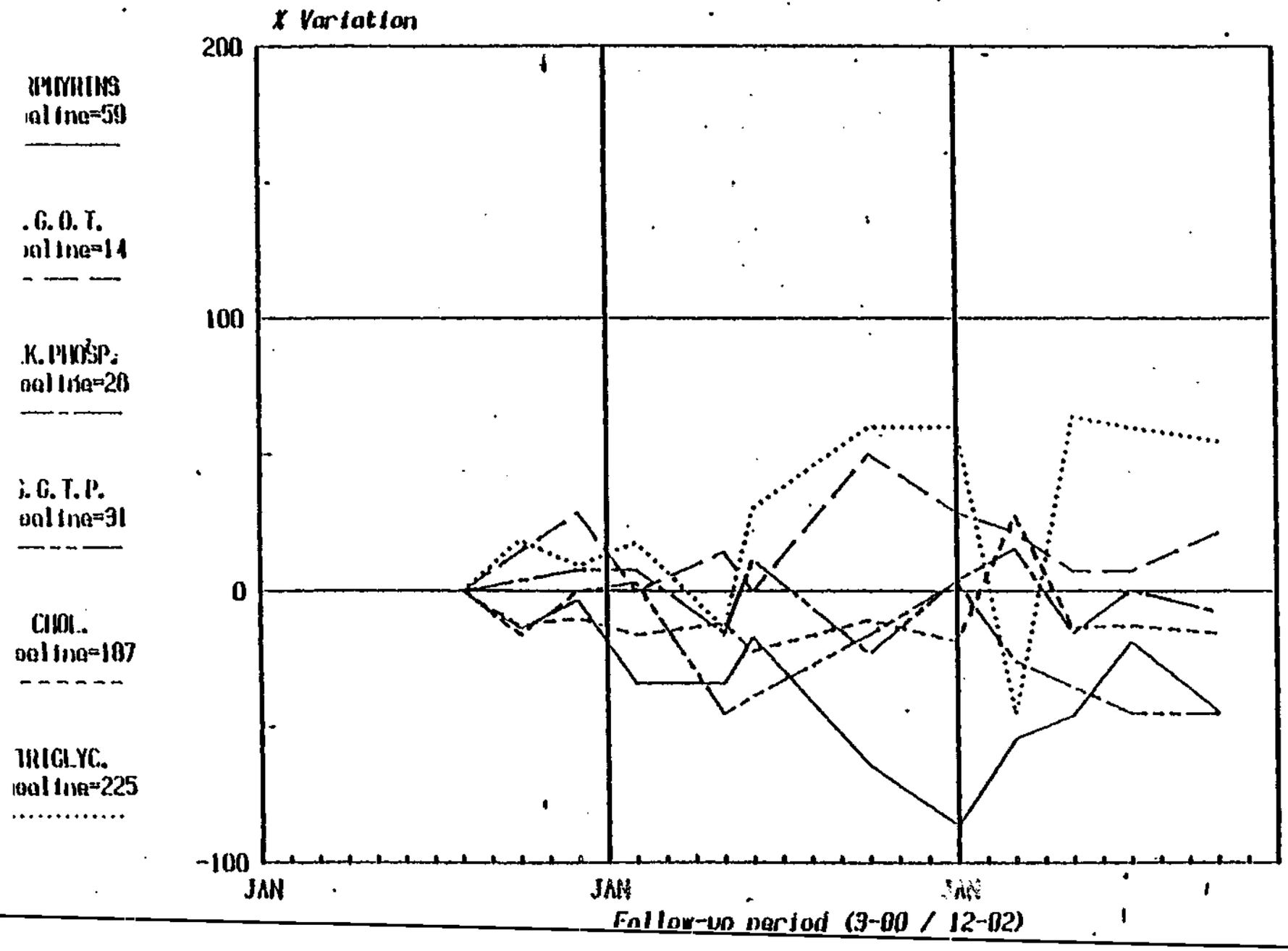
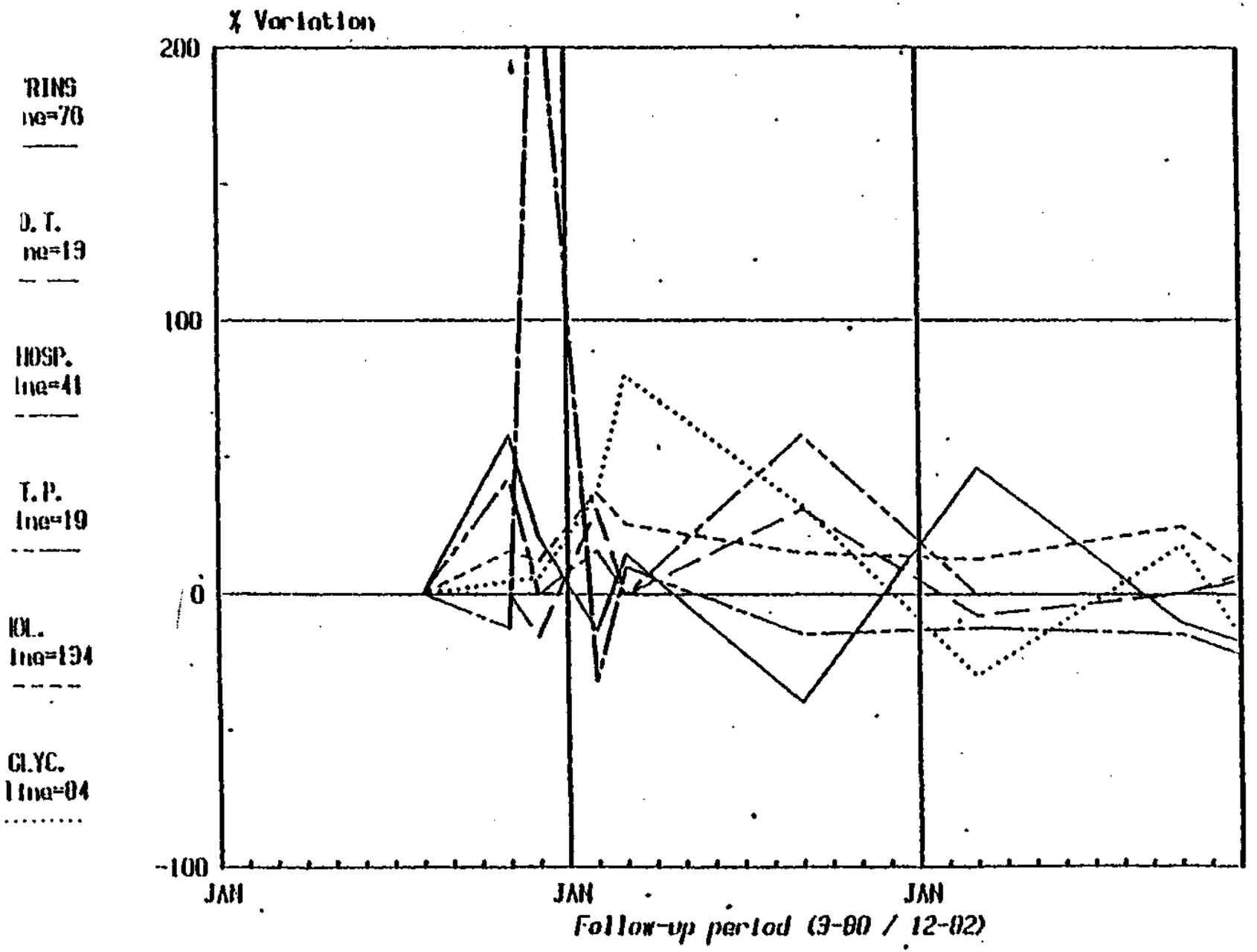


Fig.73 TIME TRENDS OF 6 PARAMETERS IN CLEAN-UP WORKER #36: A. S., 23 yrs



APPENDIX A

FACSIMILE OF INTERVIEW QUESTIONARY

Study on the surveillance of the clean-up workers in the TCDD decontamination, Seveso, Italy.

Date of the interview _____

Starting time _____

Interviewer's number _____

Interview number _____

A - Personal Data

A1 - "What is your full name?"

_____

A2 -"When were you born?" (Specify day, month and year)

_____

A3 - "Where were you born?" (Specify Town and Province)

_____

A4 -"What is your address?" (Specify street, number, Town, provi
postal code)

_____

A5- "Do you have a telephone?"

Yes ..... /__/

No ..... /__/

I don't Know ..... /__/

No answers ..... /__/

If YES, go to A6
else, go to A7

A6- "What is your telephone number?"

_____

I don't know /__/

A7 - "What is your present civil status?"

Single ..... /__/
Married ..... /__/
Separated ..... /__/
Divorced ..... /__/
Widow/er ..... /__/
Other (specify) .....
..... /__/
No answers ..... /__/

A8 - "What is the highest educational record you have got?"

University degree ..... /__/
High School ..... /__/
Secondary School ..... /__/
Primary School ..... /__/
Other (specify)..... /__/
No records ..... /__/
I don't know ..... /__/
No answers ..... /__/

A9 - "Did you do the military service?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
NO ANSWERS ..... /__/
OTHER (Specify) .... /__/

If NO, go to A10
else, go to A12

A10 -"Why did you not do the military service?"

Health reasons ..... /__/
Family reasons ..... /__/
Other (Specify) ..... /__/

A11 - "In the last month, have you been smoking cigarettes?"

YES ..... /__/

NO ..... /__/

I CANNOT REMEMBER .... /__/

NO ANSWERS ..... /__/

OTHER ..... /__/

If YES, go to A12

else, go to A17

A12 - "How many a day?" /__/__/

A13 - "At what age did you start smoking?"

..... /__/

I cannot remember .... /__/

No answers ..... /__/

A14 - "How long have you been smoking?"

YEARS ..... /__/__/

I CANNOT REMEMBER ... /__/

A15 - "Over the last five years, the number of cigarettes you smoke a day has:

INCREASED ..... /__/

DECREASED ..... /__/

THE SAME ..... /__/

I DON'T KNOW ..... /__/

OTHER (Specify) .....

.....

..... /__/

In case of increase or decrease, go to A16, else, go to A17.

A16 - "Why?" (Specify) .....
.....

Go to A21

A17 - "Have you ever smoked in the past?"

If yes, go to 18
else, go to A21

A18 - "How old were you when you smoked the first cigarette?"

AGE ...../__/
I CANNOT REMEMBER ..../__/

A18bis - "Have you smoked more than 5 packets of cigarettes in your life?"

If yes, go to A19
else, go to B1

YES ..... /__/
NO ..... /__/

A19 - "For how many years have you been smoking?" /__/__/

A20 - "How many cigarettes a day were you smoking in that period?"

NUMBER OF CIGARETTES ..... /__/
I CANNOT REMEMBER ..... /__/

ALCOHOL

B1 - "Have you ever drunk alcoholic drinks like wine, liquors, beer?

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
OTHER (Specify).....
..... /__/
NO ANSWERS ..... /__/

If YES, go to B2
else, go to C1

B2 - "At what age did you start drinking alcoholic beverages?"

YEARS ..... /__/__
I DON'T KNOW ..... /__/__
NO ANSWERS ..... /__/__
OTHER (Specify) .....
..... /__/__

B3 - "At present, are you drinking alcoholic beverages?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
NO ANSWERS ..... /__/

If YES, go to B6

else, go to B4

B4 - "At what age did you give up drinking alcoholic beverages?"

YEARS ..... /__/__
I DON'T KNOW ..... /__/__
NO ANSWERS ..... /__/__

B5 - "Why did you give up drinking alcoholic beverages?"

.....
.....
I DON'T KNOW ..... /__/
NO ANSWERS ..... /__/

Note for the interviewer:
read DRINKS if yes at B2, else read DRINKED

B6 - "Could you specify what kind of alcoholic beverages you usual DRINK/DRANK?"

WINE ..... /__/
BEER ..... /__/
OTHER (Specify) .....
/

REGULARLY DURING MEALS ..... /_
REGULARLY DURING AND
BETWEEN MEALS..... /_
REGULARLY BETWEEN MEALS ..... /_
I DON'T KNOW ..... /_
NO ANSWERS ..... /_

B8 - "On these occasions, how much do you drink?"

WINE ..... /__/
1-2 glasses a day ..... /__/
Two glasses to half a liter a day..... /__/
Half a liter to one liter a day ..... /__/
More than one liter a day ..... /__/
I don't know ..... /__/
No answers ..... /__/

BEER ..... /__/
1-2 glasses a day ..... /__/
Two glasses to half a liter a day ..... /__/
Half a liter to one liter a day ..... /__/
More than one liter a day ..... /__/
I don't know ..... /__/
No answers ..... /__/

B9 - "Have you been drinking these drinks in the last week?: Whisky, Brandy, Bitters, etc.?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
NO ANSWERS ..... /__/

If YES, go to B10
else go to C1

B10 - "What kind of hard liquors have you drunk?"

ALCOHOLIC APERITIFS ..... /__
BITTERS-DIGESTIVES ..... /__
EAU-DE-VIE..... /__
COGNAC ..... /__
WHISKY ..... /__
COFFEE WITH LIQUEUR ..... /__
OTHER:.....
..... /__

B11 - "You usually drink these drinks:

OCCASIONALLY ..... /__/
REGULARLY BEFORE OR AFTER MEALS ..... /__/
REGULARLY BETWEEN MEALS ..... /__/
REGULARLY BOTH ON AND BETWEEN MEALS ..... /__/

B12 - "On these occasions, how much do you drink?"

ONE TO TWO LIQUEUR GLASSES A DAY..... /__/
THREE TO FOUR LIQUEUR GLASSES A DAY..... /__/
MORE THAN FOUR LIQUEUR GLASSES A DAY..... /__/

C1 - "In the last two months from today, have you been taking medi
pills, suppositories, syrups, etc.

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
NO ANSWERS ..... /__/

If YES, go to C2
else, go to D1

C2 - "Would you please tell the names of the medicines you have taken

1) _____
2) _____
3) _____
4) _____

For each medicine at C2,
go to the questions C3,C4,C5

C3 - "Have you been taking 1), 2), 3), 4) for more than one week?"

	1)	2	3	4
YES	/__/	/__/	/__/	/
NO	/__/	/__/	/__/	/
I DON'T KNOW	/__/	/__/	/__/	/
NO ANSWERS	/__/	/__/	/__/	/

C4 - "What troubles caused you to take 1), 2), 3), 4)?"
Note: Specify the type of trouble for each medicine

1) .....
2) .....
3) .....
4) .....

C5 - "Did the physician prescribe the medicine 1), 2), 3), 4)?"

	1) /__/	2) /__/	3) /__/	4) /__/
YES	/__/	/__/	/__/	/__/
NO	/__/	/__/	/__/	/__/
I DON'T KNOW .	/__/	/__/	/__/	/__/
NO ANSWERS ...	/__/	/__/	/__/	/__/

C6 - "For how long have you been taking the medicine 1), 2), 3), 4)?"

	YEARS	MONTHS
1)	/__/__/	/__/__/
2)	/__/__/	/__/__/
3)	/__/__/	/__/__/
4)	/__/__/	/__/__/

D1 - MEDICAL HISTORY

"Have you ever suffered from any of the following troubles or diseases?"

	YES	NO	I DON'T REM.	I DON'T KNOW	YEAR OF ST.
Acne	/__/	/__/	/__/	/__/	/__/
Boils	/__/	/__/	/__/	/__/	/__/
Viral hepatitis	/__/	/__/	/__/	/__/	/__/
Chronic hepatitis	/__/	/__/	/__/	/__/	/__/
Hepatic cirrhosis	/__/	/__/	/__/	/__/	/__/
Epilepsy	/__/	/__/	/__/	/__/	/__/
Gall-bladder and/or biliary ducts stones	/__/	/__/	/__/	/__/	/__/
Diabetes	/__/	/__/	/__/	/__/	/__/

For each YES at D1, ask for D2 and fill in the above column, else go to D3

D2 - "When did it start ..... (read the disease)?"

D3 - "Have you ever been hospitalized?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
NO ANSWERS ..... /__/

If YES go to D4, else go to D9

D4 - "How many times have you been hospitalized?"

Number of times /__/

D5 - For each time, write the disease, the year, the Hospital name and the town where it is.

"For what disease have you been hospitalized the (1st, 2nd, 3rd) time?

D6 - "When did it happen?" (year)

D7 - "What is the name of the Hospital?"

D8 - "Where is the Hospital?" (town)

Disease	Number of Hospitalizations	Year of Hospitalization	Hospital Name	
.....	.....	.....	.....	...
.....	.....	.....	.....	...
.....	.....	.....	.....	...
.....	.....	.....	.....	...
/	/	/	/	

D9 - "Please, tell us the name and the address of your physician"

.....

D10 - "Have your physician ever told you that your liver is in ba conditions?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
I DON'T REMEMBER .... /__/

D11 - "In the last two years, have you ever lost more than 5 Kilos without being on a special diet?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
I DON'T REMEMBER ..... /__/

If YES go to D12, else go to D13

D13 - "Why did you lose weight?"

.....

D13 - "In the last two years have you ever been under treatment again. anaemia?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
I DON'T REMEMBER ..... /__/
NO ANSWERS ..... /__/

If YES specify the treatment

D14 - "Have you ever suffered from skin troubles because of exposure sunbeams?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/
NO ANSWERS ..... /__/

If YES go to D15 else go to E1

D15 - "Please describe these troubles"

.....

D16 - "Do these troubles reappear after each exposure to sunbeams?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/

ENDING TIME OF THE QUESTIONNAIRE /__/__/__/__/

E1 - " Is the interviewed hard of hearing?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/

E2 - "Can the interviewed speak and understand Italian correctly?"

YES ..... /__/
NO ..... /__/
I DON'T KNOW ..... /__/

E3 - "In which day of the week was the interview made?"

Monday /__/
Tuesday /__/
Wednesday /__/
Thursday /__/
Friday /__/

APPENDIX B

CASE SHEET USED FOR MEDICAL EXAMINATION

DESIO HOSPITAL

OCCUPATIONAL HEALTH SERVICE

Chief Physician: Prof. I.Ghezzi

CLINICO-EPIDEMIOLOGICAL SURVEY

MDL - 1 ICMESA
MDL - 2 CLEAN-UP WORK

Desio Hospital .....

Surname and name

Place of birth date

Registered residence tel.

Usual address

Marital status

married urmarried widower separated divorced

Occupation

Exposed control

Treating physician

Examining physician

FAMILY HISTORY

Father

Mother

Siblings

Wife

PHYSIOLOGICAL HISTORY

Birth	at term	premature	
Delivery	normal	dystocic	twin
Development	normal	precocious	late
Schooling	compulsory	high school	university

Military service:

yes force

no health reasons :

yes

no

Marriage: no

yes at ... years

no. children

no. abortions

Present occupation

Previous "

(for risks see questionary)

smoking (see questionary)
drinking (see questionary)
drugs (see questionary

} only additions, if any

Diet

poor normal plentiful

Digestion: normal yes
no why

Bowel movements: normal constipated loose

Urine output: normal yes
no why

Sex life:

reported normal
reported abnormal since which year
why

PAST HISTORY: (supplemented by questionary)

Diseases:

Hospital admissions

Accidents

Allergies

PRESENT HISTORY: (past year)

Visual apparatus
- disturbances
- diseases

Auditory apparatus
- disturbances
- diseases

Respiratory system
- disturbances
- diseases

Heart
- disturbances
- diseases

Digestive tract
- disturbances
- diseases

Urinary system

disturbances

diseases

Limbs

disturbances

diseases

Musculoskeletal system

disturbances

diseases

Skin

disturbances

diseases

Nervous system

disturbances

diseases

PHYSICAL EXAMINATION

Height Weight kg Usual weight

Constitution:

longilineal	normal	brevilineal	athletic
thin	medium	fat	obese

BP max min Heart rate

Skin: normal
abnormal
specialist examination

Subcutaneous tissue. Abnormal findings
no
yes which

Lymph nodes. Abnormal findings
no
yes specify

Musculature. Abnormal findings
no
yes specify

Skeletal system. Abnormal findings
no
yes specify

Head: mobility ache yes
no

eyes abnormal findings no
yes

ears: abnormal findings no
nose:
yes

mouth: oropharynx abnormal findings no
yes

teeth abnormal findings no
yes

Neck: abnormal findings no
yes

Respiratory System: abnormal findings no
yes

if yes: chest deformity
F.V.T. (fremitus - vocal - tactile)
percussion
auscultation

Mammary Glands: abnormal findings no
yes

Heart: abnormal findings no yes
if yes:

Abdomen: abnormal findings no

yes

Liver: normal findings yes no

in any case:

- upper limit on the right midclavicular line:

  intercostal space or rib

- lower limit (cm from the costal arch on right midclavicular line):

. at end of normal inspiration

palpation

percussion

. in max forced inspiration

palpation

percussion

- margin and surface
- consistency
- tenderness

Spleen: normal findings yes no

Other Findings Abdominal Organs

Genitourinary System

Kidneys: abnormal findings no yes

Bladder: abnormal findings no yes

External genitalia: abnormal findings no yes

Limbs: abnormal findings no yes

upper

lower

varices no yes

peripheral pulses (radial, posterior tibial, dorsal artery of foot)

abnormal findings

no yes

if yes:

Nervous System And Psyche

abnormal findings no yes

Remarks: