

# Trace Elements in Relation to Cardiovascular Disease\*•

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CARDIOVASCULAR disease may be considered as a public health problem in the Philippines. Reports of the Disease Intelligence Center, Department of Health show that diseases of the heart has a five year average mortality rate of 35.2 per 100,000 population and constitute 5.1% of the total deaths in the Philippines. In the search for the etiologic factors of cardiovascular disease one has to consider the role of trace elements. In our previous reports<sup>1,2</sup> we reported an increase in the mean values of manganese and copper and a decrease in the mean levels of zinc in the serum of patients with hypertension, old myocardial infarct and diabetes mellitus. Kana-brocki<sup>3</sup> and Wacker<sup>4</sup> also suggested the possible relationship of copper, zinc and manganese to cardiovascular disease. In the present report we shall present findings on the concentration of copper, zinc and molybdenum in the heart, liver and

kidneys of 20 normal male healthy subjects that met accidental death and from 25 male patients who died of myocardial infarction.

## MATERIALS AND METHODS

Samples that were analyzed for their trace elemental contents were taken from the anterior wall of the left ventricle, the superior anterior surface of the right lobe of the liver, and the cortex of the kidney. During the collection of the samples, extreme care was taken to prevent metallic contamination with the use of glass or silica knives. Preparation of irradiation standards for copper, zinc and molybdenum, as well as the biological reference materials to check the accuracy of our analytical procedures has been previously described<sup>2</sup>. Preparation of the tissue samples for irradiation and the determination of its trace metals contents by neutron activation technique has already been reported<sup>5</sup>.

## RESULTS AND DISCUSSION

Figures I, II and III will show the gamma ray spectrum of zinc, copper and molybdenum in the heart, liver and kidney. The results in Tables I to III indicate the values of copper, zinc and

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molybdenum in the heart, liver and kidney of normal male subjects that met accidental death. The results in Table IV show that the mean values of zinc, copper and molybdenum in the heart, liver and kidneys of Pilipinos are agreeable to the mean values reported in literature. The results in Tables I to III also indicate that the normal values of copper, zinc and molybdenum in the heart, liver and kidneys of the normal subjects do not vary with their age and occupation. Figures IV to XII will show the scattergram of zinc, copper and molybdenum levels obtained from heart, liver and kidney tissues of normal healthy subjects and patients with myocardial infarction. The results in Table V indicate that the mean concentration of zinc in the heart and liver of patients who died of myocardial infarction,  $28.85 \pm 2.07$  ug/g and  $37.57 \pm 8.38$  ug/g respectively were lower than the normal mean values of  $30.35 \pm 2.33$  ug/g and  $47.30 \pm 7.72$  ug/g. Our data on the decrease of zinc concentration in the infarcted heart tissue is in good agreement with the report of Wester<sup>6</sup>, who reported a significant decrease of zinc level in the injured heart tissues. This decrease might perhaps be related to the disappearance of lactic dehydrogenase, a zinc enzyme from the infarcted heart tissue with an increase in the level of its activity being observed in the serum of patients with acute myocardial infarction<sup>7</sup>. Zinc has been reported to be beneficial to cardiovascular health. Schroeder<sup>8</sup> found that the administration of zinc will reverse the hypertensive effect of cadmium in rats. The mean level of copper in the liver of patients with myocardial infarction of  $3.95 \pm 0.82$  ug/g was lower than the normal value of  $5.01 \pm 1.96$  ug/g. Hartman<sup>9</sup> has reported the atherogenic effect of copper. Reinhold<sup>10</sup>

found that a deficiency in copper would also result in the defective synthesis of collagen and elastin in the aorta and blood vessels. The mean concentration of molybdenum,  $0.83 \pm 0.13$  ug/g,  $0.76 \pm 0.36$  ug/g and  $0.74 \pm 0.31$  ug/g in the heart, liver and kidney respectively of patients with myocardial infarction were higher than the normal values of  $0.32 \pm 0.13$  ug/g,  $0.52 \pm 0.16$  ug/g and  $0.41 \pm 0.20$  ug/g. Our data on the molybdenum content of the infarcted heart tissue does not agree with the results obtained by Wester<sup>7</sup> who reported a decrease in the concentration of molybdenum in the injured heart tissue, and relate the concentration of this trace element to the degree of fibrosis present in the infarcted heart tissue.

The data that we have obtained our 5 years investigation indicate changes in the concentration of copper, zinc and molybdenum in the heart, liver and kidney of cardiac subjects occurring in association with myocardial infarction. We do hope that the tissue mineral concentration changes that we detected will add significant data to the growing evidence that certain trace elements are associated with degenerative cardiovascular diseases, such as hypertension, atherosclerosis and their sequela. The results that we obtained would not only help in establishing the elemental composition of a "Standard Man" but this study might give us a clue on the biochemical association of the certain trace elements with cardiovascular disease, which would offer information of importance in the control of this public health problem.

#### SUMMARY

Heart, liver and kidney specimens from 45 adult male subjects were analyzed for their zinc, copper and molyb-

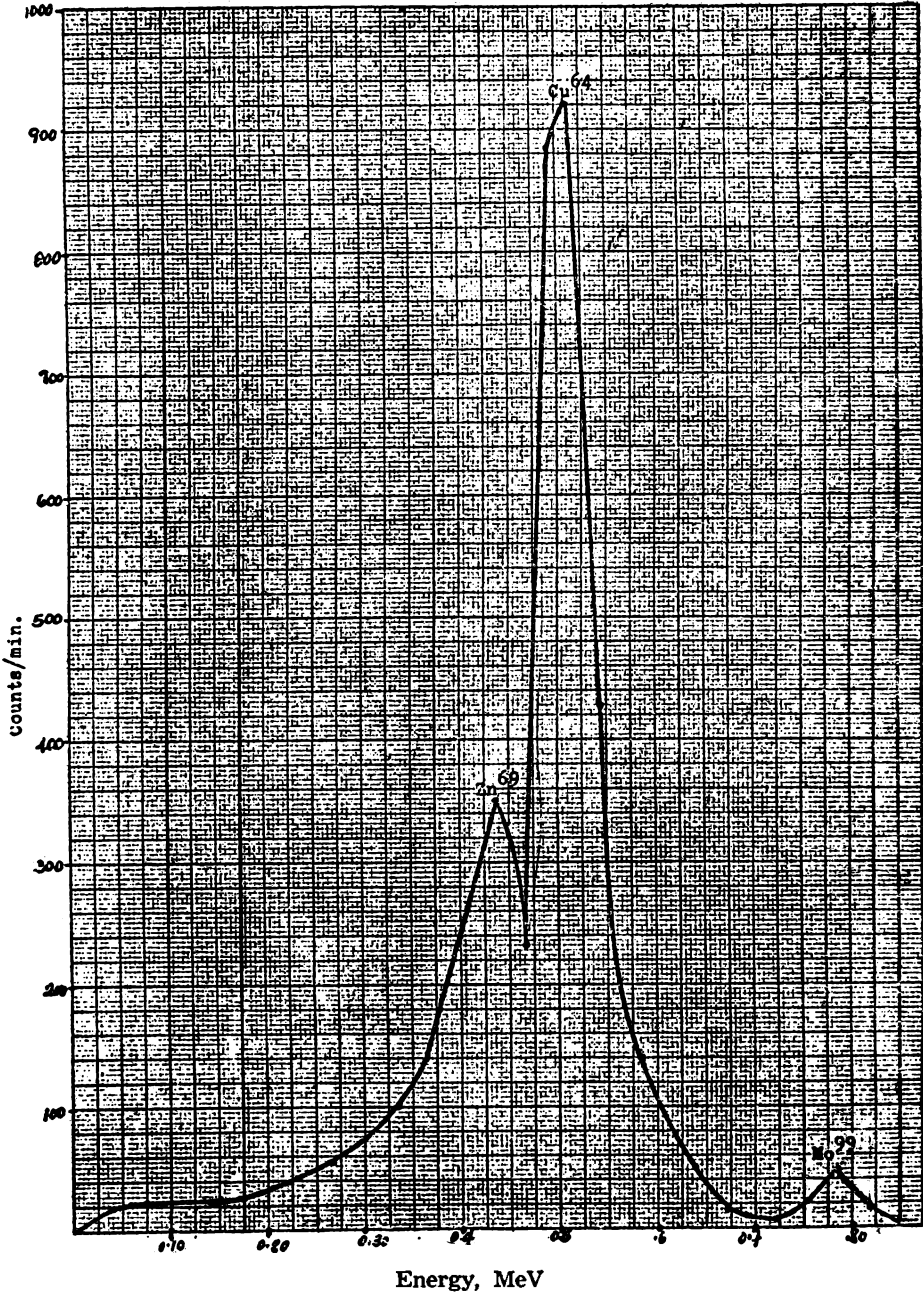


Fig. 1 — Gamma-ray spectrum of Zinc, Copper and Molybdenum in Heart.

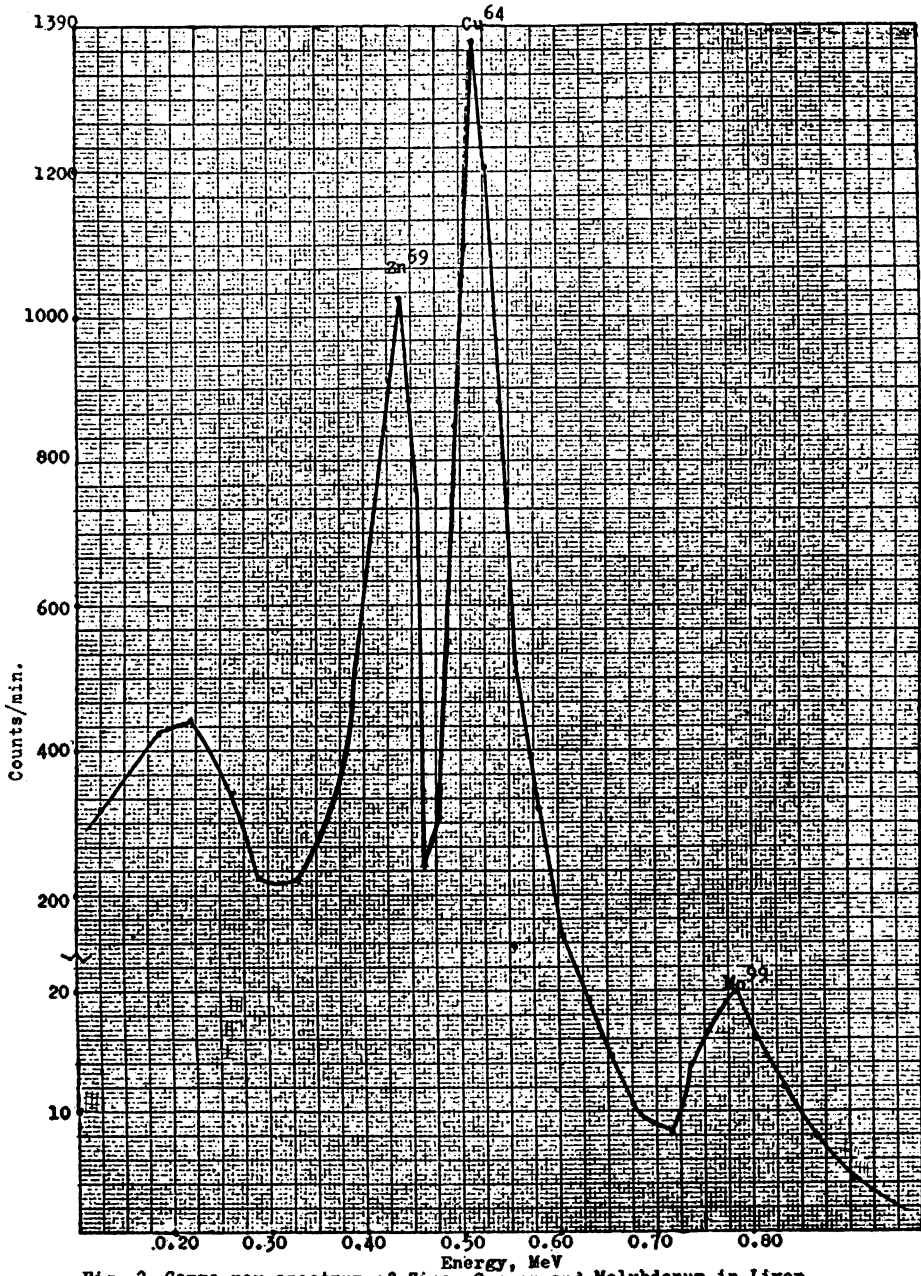


Fig. 2- Gamma-ray spectrum of Zinc, Copper and Molybdenum in Liver

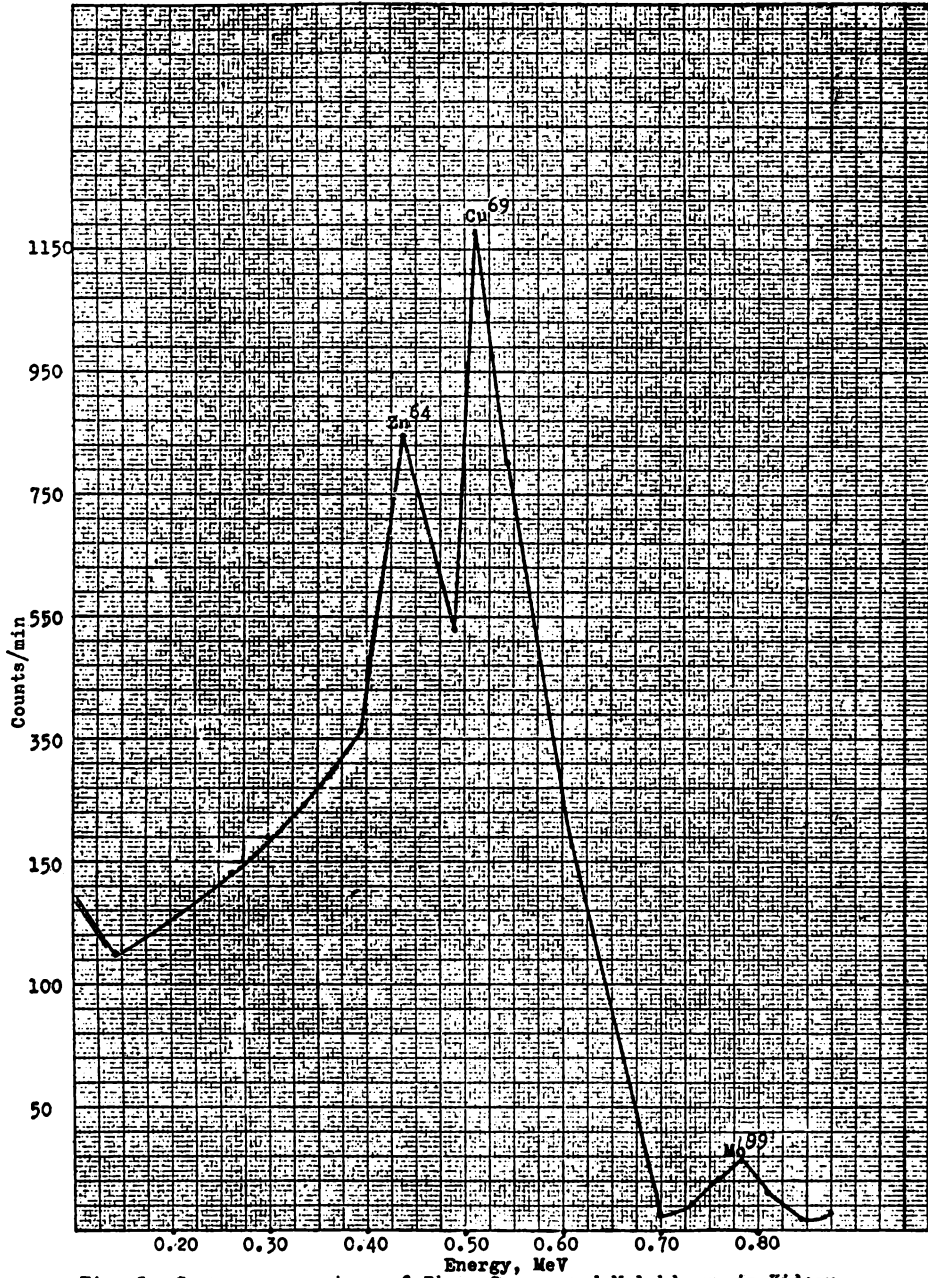
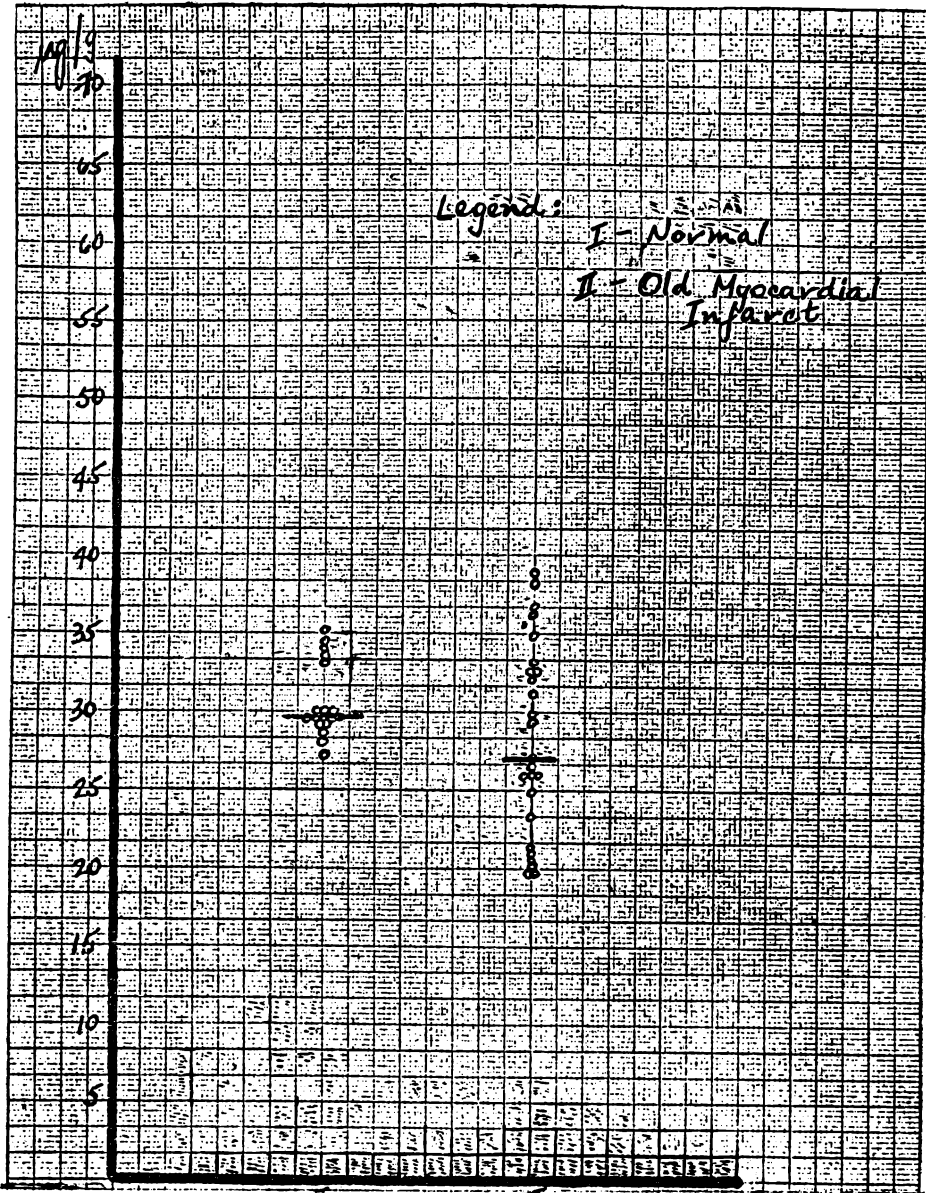


Fig. 3 - Gamma-ray spectrum of Zinc, Copper and Molybdenum in Kidney



I II

Fig. 4 — Scattergram of zinc levels obtained from heart tissues of normal subjects and patients with old myocardial infarct.

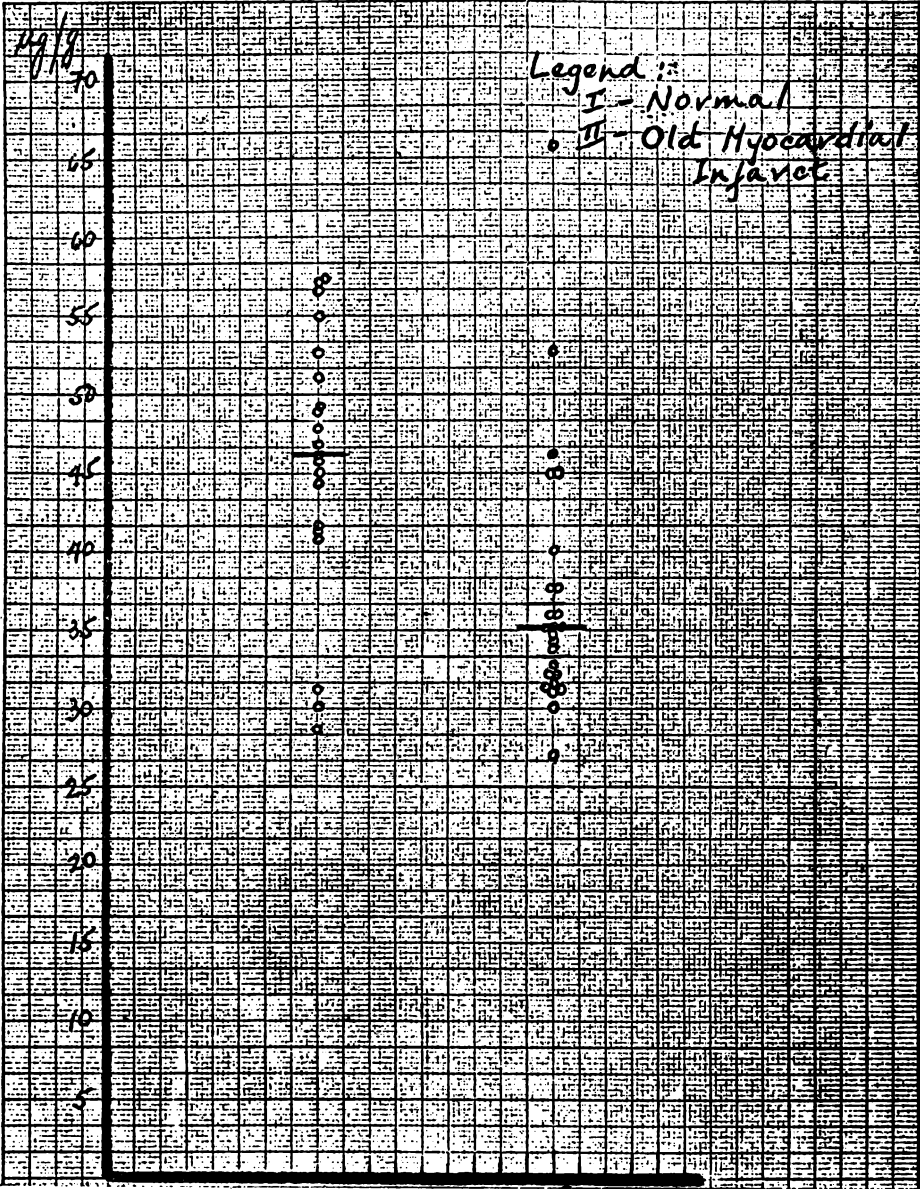


Fig. 5 — Scattergram of zinc levels obtained from liver tissues of normal subjects and patients with old myocardial infarct.

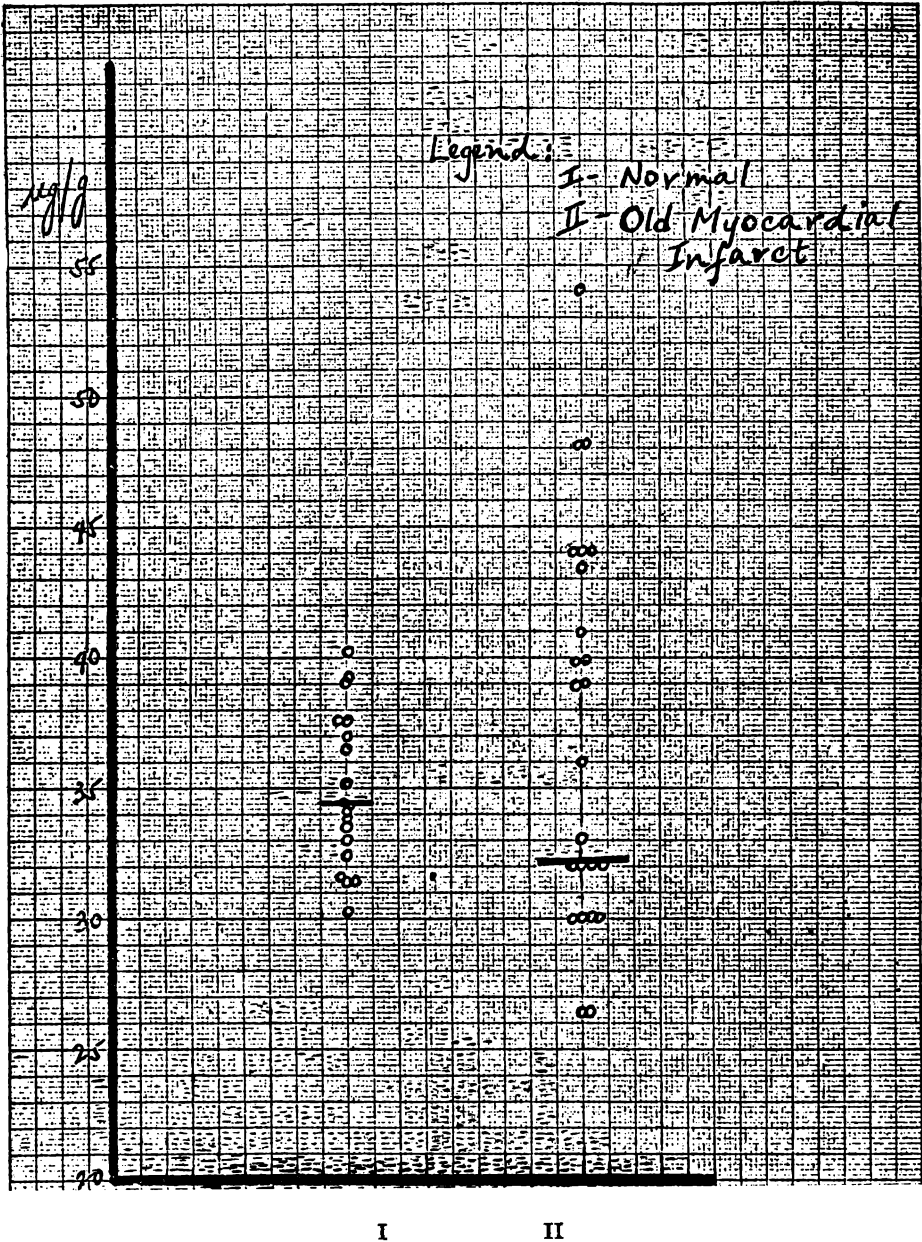


Fig. 6 — Scattergram of zinc levels obtained from kidney tissues of normal subjects and patients with old myocardial infarct.



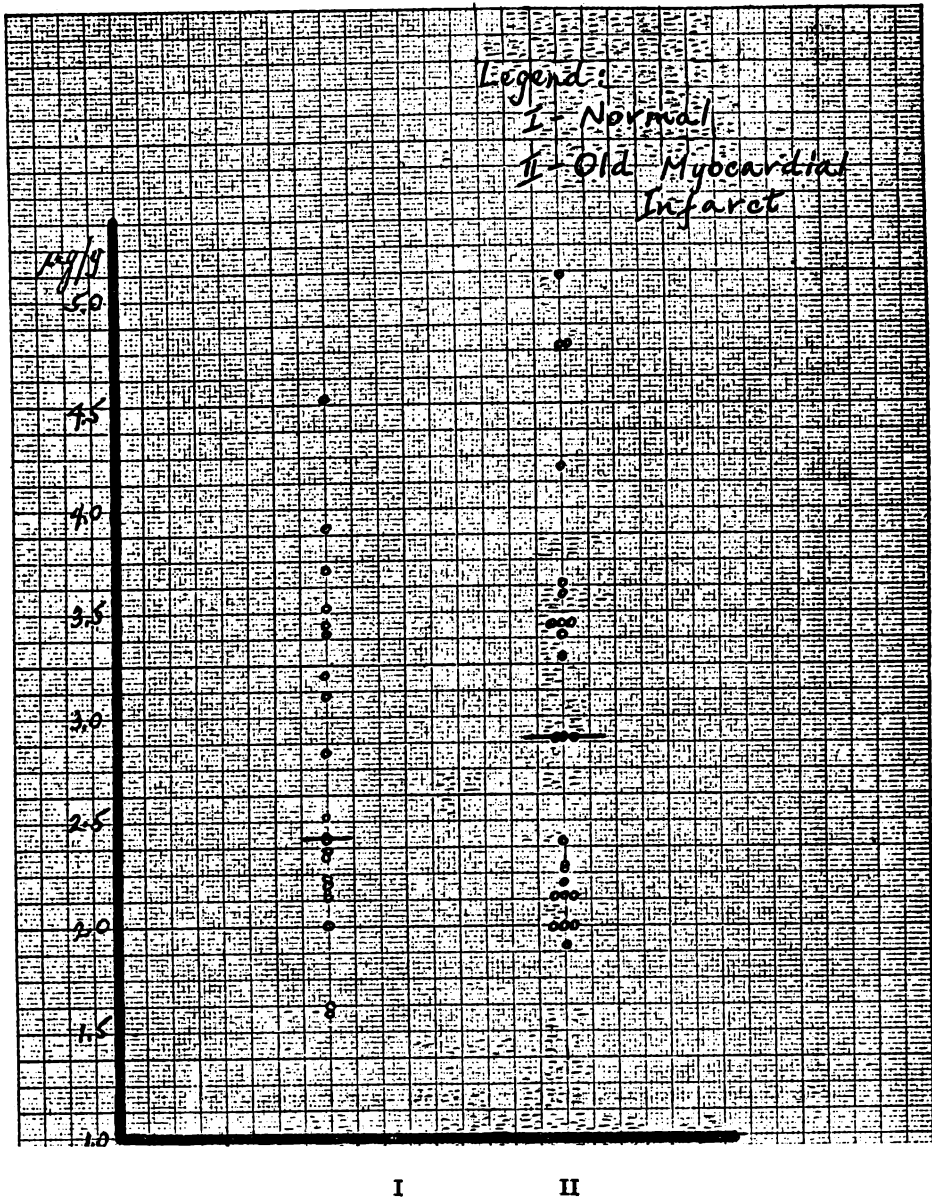


Fig. 7 — Scattergram of copper levels obtained from heart tissues of normal subjects and patients with old myocardial infarct.

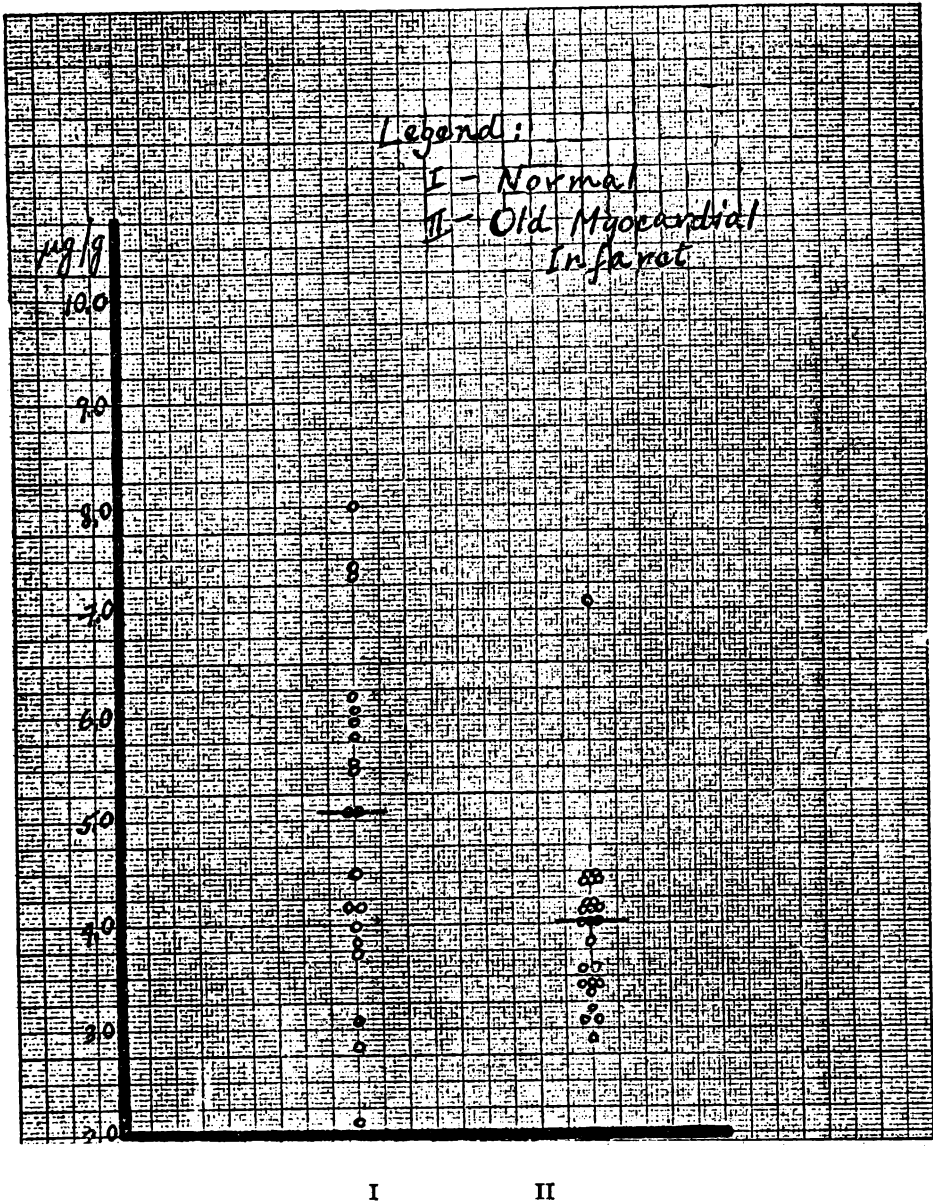


Fig. 8 — Scattergram of copper levels obtained from liver tissues of normal subjects and patients with old myocardial infarct.

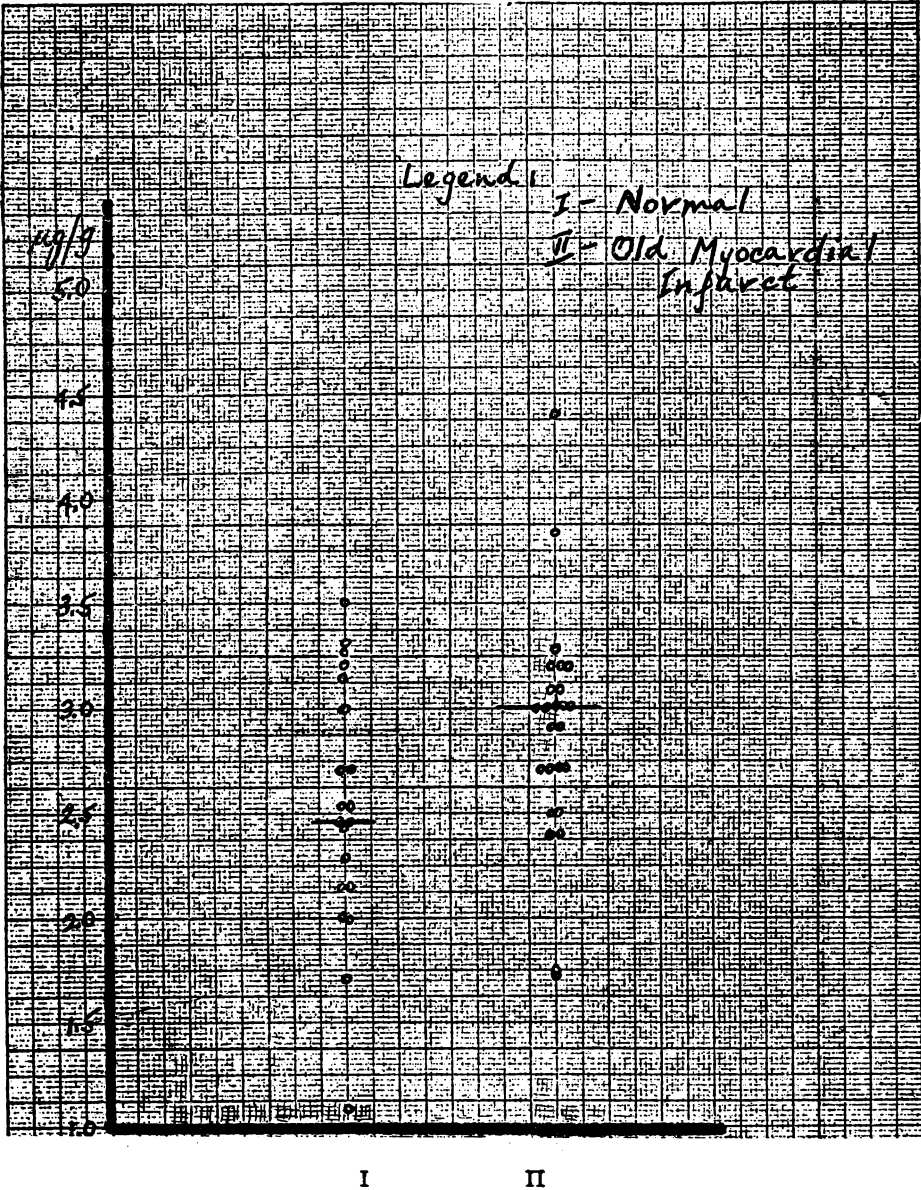


Fig. 9 — Scattergram of copper levels obtained from kidney tissues of normal subjects and patients with old myocardial infarct.

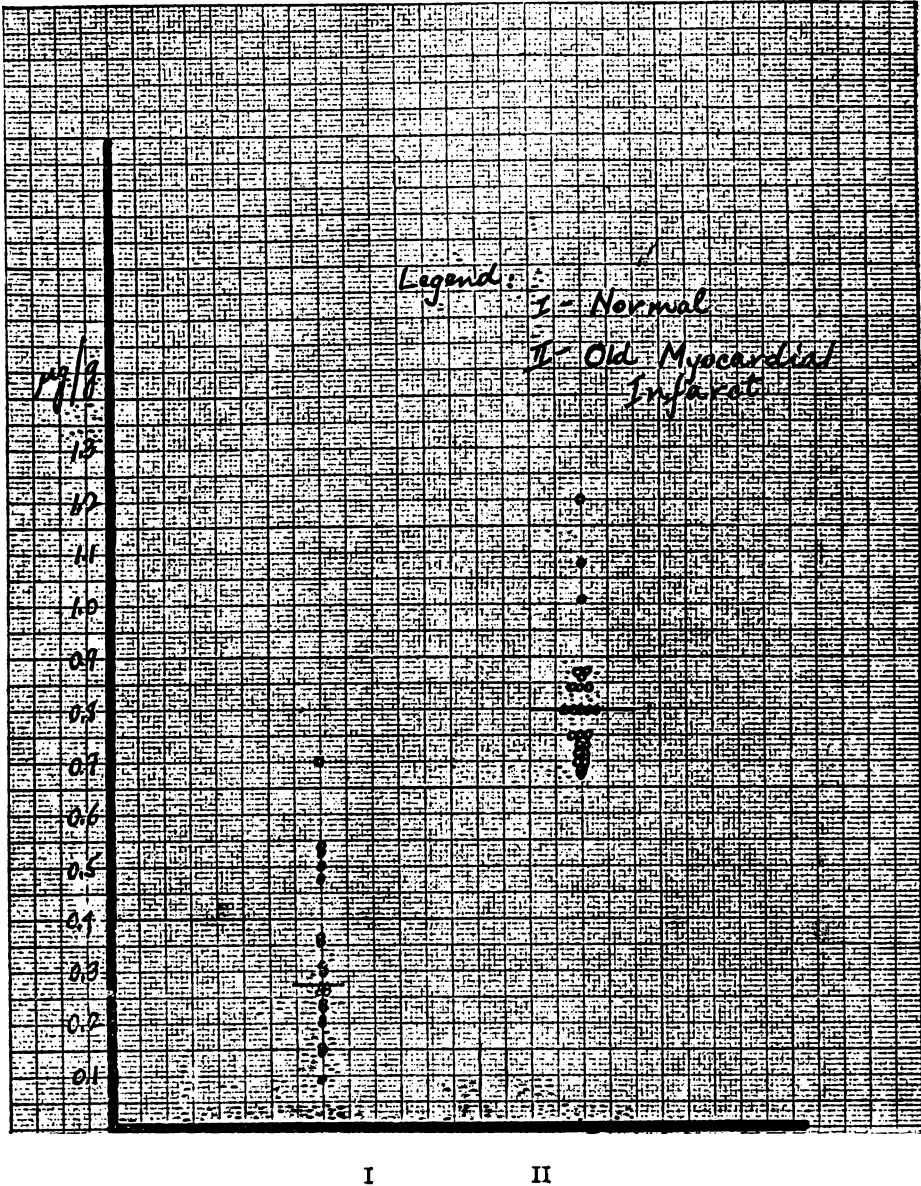


Fig. 10 — Scattergram of molybdenum levels obtained from heart tissues of normal subjects and patients with old myocardial infarct.

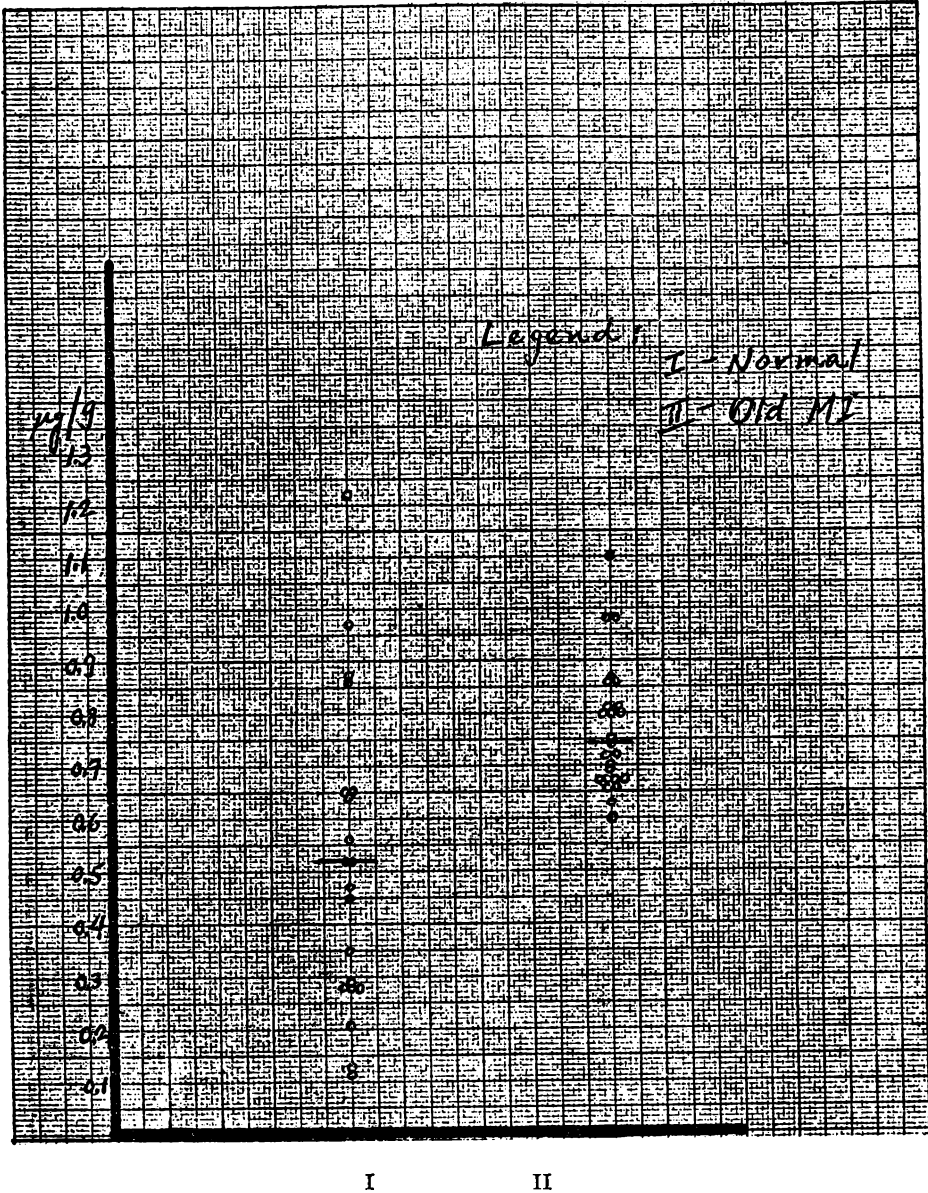


Fig. 11 — Scattergram of molybdenum levels obtained from liver tissues of normal subjects and patients with old myocardial infarct.

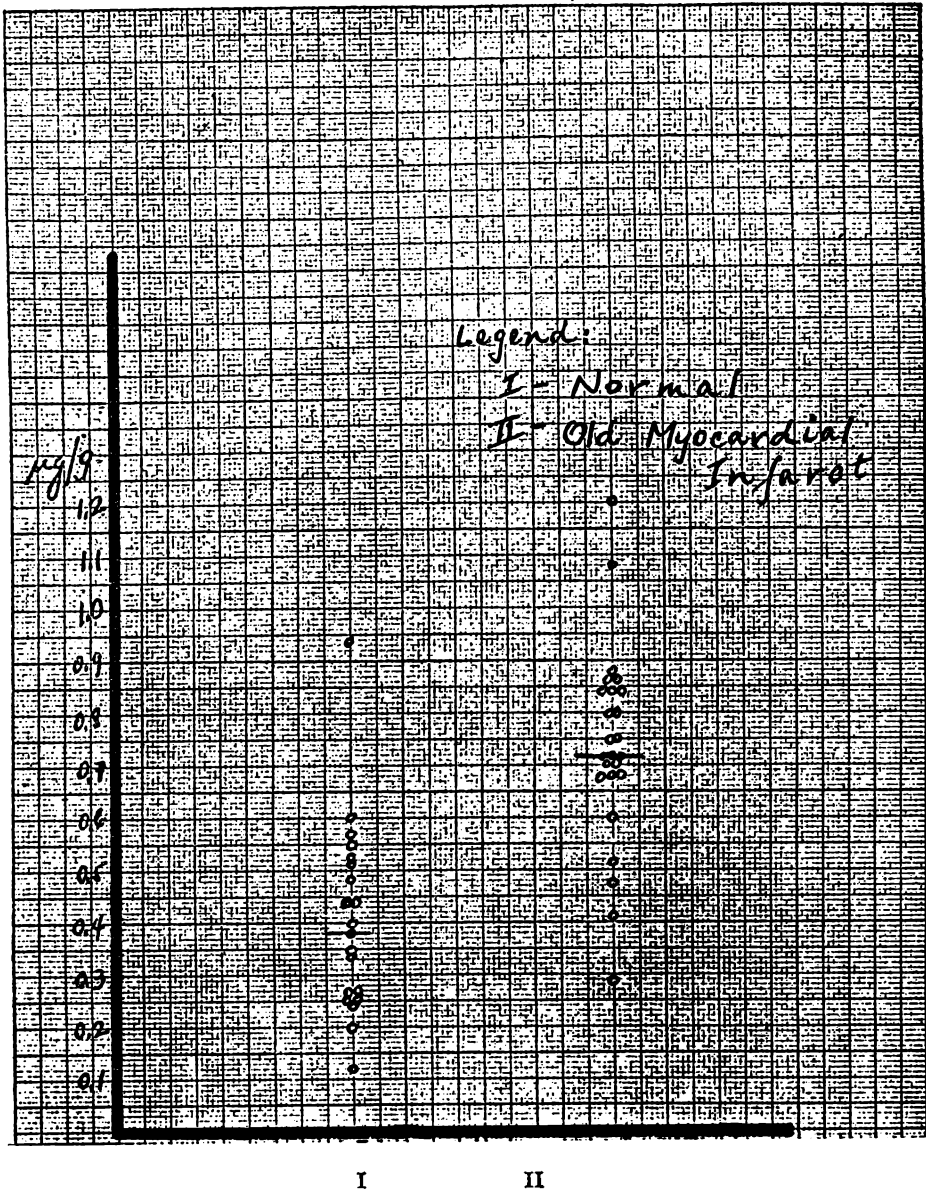


Fig. 12 -- Scattergram of molybdenum levels obtained from kidney tissues of normal subjects and patients with old myocardial infarct.

**Table I. VALUES OF ZINC IN HEART, LIVER AND KIDNEY OF 20 NORMAL MALE SUBJECTS: ug/g WET TISSUE**

Name	Age	Occupation	Cause of Death	Heart	Liver	Kidney
O. D.	40	Soldier	Vehicular accident	30.50	44.50	39.30
R. J.	40	Vendor	Stabbing	29.50	46.00	33.55
Unknown	40	N. A.	Gunshot wound	28.55	40.67	31.83
Unknown	40	N. A.	Stabbing	32.70	49.00	33.20
F. S.	43	Butcher	Stabbing	30.07	45.40	33.89
R. S.	45	Businessman	Stabbing	29.04	42.30	37.10
L. S.	45	Patrolman	Stabbing	30.50	57.45	31.64
F. C.	45	Scavenger	Vehicular accident	26.86	47.80	36.78
H. C.	45	Laborer	Vehicular accident	29.64	28.13	35.48
J. B.	45	Employee	Stabbing	29.64	54.41	35.03
A. P.	45	Driver	Vehicular accident	33.60	41.60	32.53
M. L.	46	Employee	Stabbing	35.29	30.66	37.69
N. C.	47	Driver	Vehicular accident	28.26	55.30	31.68
M. J.	43	Security	Gunshot	33.00	57.64	30.20
		Guard				
A. T.	48	Employee	Vehicular accident	30.19	51.61	34.26
P. D.	48	Security	Karate blow	28.60	32.20	34.40
		Guard				
S. T.	48	None	Vehicular accident	34.80	48.63	40.27
A. D.	48	Employee	Gunshot	27.82	46.90	37.69
M. L.	50	Realtor	Gunshot	29.26	57.41	34.68
A. C.	54	Operator	Stabbing	29.10	49.20	39.20

**Table II. VALUES OF COPPER IN HEART, LIVER AND KIDNEY OF 20 NORMAL MALE SUBJECTS; ug/g WET TISSUE**

Name	Age	Occupation	Cause of Death	Heart	Liver	Kidney
O. D.	40	Soldier	Vehicular accident	3.10	2.80	3.40
R. J.	40	Vendor	Stabbing	2.02	7.41	2.15
Unknown	40	N. A.	Gunshot	2.19	8.00	2.48
Unknown	40	N. A.	Stabbing	1.62	3.10	2.00
F. S.	43	Butcher	Stabbing	2.20	7.60	2.54
R. S.	45	Businessman	Stabbing	2.43	6.20	2.99
L. S.	45	Patrolman	Stabbing	3.20	5.66	2.01
F. C.	45	Scavenger	Vehicular accident	4.54	5.49	2.72
H. C.	45	Laborer	Vehicular accident	3.26	3.79	1.71
J. B.	45	Employee	Stabbing	1.60	4.14	2.54
A. P.	45	Driver	Vehicular accident	3.40	5.13	3.15
M. L.	46	Employee	Stabbing	3.86	5.14	2.69
N. S.	47	Driver	Vehicular accident	2.84	6.02	2.46
		Security	Gunshot	3.45	4.00	3.44
M. J.	43	Guard				
A. T.	48	Employee	Vehicular accident	2.45	4.49	2.15
P. D.	48	Security	Karate blow	2.30	5.90	1.10
		Guard				
S. T.	48	None	Vehicular accident	3.62	5.32	3.51
A. D.	48	Employee	Gunshot	2.40	4.12	2.32
M. L.	50	Realtor	Gunshot	2.52	2.12	2.48
A. C.	54	Operator	Stabbing	3.52	3.75	3.19

**Table III.** VALUES OF MOLYBDENUM IN HEART, LIVER AND KIDNEY OF  
20 NORMAL MALE SUBJECTS ug/g WET TISSUE

<b>Name</b>	<b>: Age</b>	<b>: Occupation</b>	<b>: Cause of Death</b>	<b>: Heart</b>	<b>: Liver</b>	<b>: Kidney</b>
O. D.	: 40	: Soldier	: Vehicular accident	: 0.15	: 0.12	: 0.48
R. J.	: 40	: Vendor	: Stabbing	: 0.23	: 0.87	: 0.60
Unknown	: 40	: N. A.	: Gunshot	: 0.21	: 0.47	: 0.25
Unknown	: 40	: N. A.	: Stabbing	: 0.48	: 0.97	: 0.52
F. S.	: 43	: Butcher	: Stabbing	: 0.70	: 0.56	: 0.51
R. S.	: 45	: Businessman	: Stabbing	: 0.54	: 0.65	: 0.57
L. S.	: 45	: Patrolman	: Stabbing	: 0.31	: 0.28	: 0.20
F. C.	: 45	: Scavenger	: Vehicular accident	: 0.31	: 0.29	: 0.12
H. C.	: 45	: Laborer	: Vehicular accident	: 0.50	: 0.45	: 0.27
J. B.	: 45	: Employee	: Stabbing	: 0.24	: 0.21	: 0.34
A. P.	: 45	: Driver	: Vehicular accident	: 0.27	: 0.52	: 0.44
M. L.	: 46	: Employee	: Stabbing	: 0.27	: 0.13	: 0.24
N. C.	: 47	: Driver	: Vehicular accident	: 0.36	: 0.35	: 0.38
M. J.	: 48	: Security Guard	: Gunshot :	: 0.09	: 0.86	: 0.35
A. T.	: 48	: Employee	: Vehicular accident	: 0.37	: 1.22	: 0.94
P. D.	: 48	: Security Guard	: Karate blow :	: 0.53	: 0.64	: 0.55
S. T.	: 48	: None	: Vehicular accident	: 0.26	: 0.28	: 0.27
A. D.	: 48	: Employee	: Gunshot	: 0.20	: 0.65	: 0.44
M. L.	: 50	: Realtor	: Gunshot	: 0.16	: 0.28	: 0.25
A. C.	: 54	: Operator	: Stabbing	: 0.26	: 0.52	: 0.40



Table IV. COMPARISON OF MEAN NORMAL VALUES OF ZINC, COPPER AND MOLYBDENUM IN THE HEART, LIVER AND KIDNEY OF FILIPINOS WITH REPORTED LITERATURE DATA; ug/g WET TISSUE

Elements	Values of Filipinos			Reported literature values*		
	Heart	Liver	Kidney	Heart	Liver	Kidney
Zinc	30.35 ± 2.33	47.30 ± 7.72	35.02 ± 2.92	20-49(3)	26-68(6)	14-67(5)
Copper	2.88 ± 0.78	5.01 ± 1.96	2.55 ± 0.62	1.9-4.4(4)	5-25(9)	0.03-3.5(6)
Molybdenum	0.32 ± 0.13	0.52 ± 0.26	0.41 ± 0.20	0.05-0.23(2)	1.6(1)	0.03-63(2)

\*Source Kollmer, W. E. et al GSF-Report B 385 (1972)  
The number of literature reports on which each range is based is given in parenthesis.

Table V. CONCENTRATION OF ZINC, COPPER AND MOLYBDENUM IN THE HEART, LIVER AND KIDNEY OF NORMAL SUBJECTS AND OF PATIENTS WITH MYOCARDIAL INFARCTION; ug/g WET TISSUE

Elements	Normal subjects			Patients with myocardial infarction		
	Heart	Liver	Kidney	Heart	Liver	Kidney
Zinc	30.35 ± 2.33	47.30 ± 7.72	35.02 ± 2.92	28.85 ± 2.07	37.57 ± 8.38	37.7 ± 7.31
Copper	2.88 ± 0.78	5.01 ± 1.96	2.55 ± 0.62	3.01 ± 1	3.95 ± 0.82	2.83 ± 0.55
Molybdenum	0.32 ± 0.13	0.52 ± 0.16	0.41 ± 0.20	0.83 ± 0.13	0.76 ± 0.36	0.74 ± 0.31

denum contents. The normal mean values of zinc, copper and molybdenum in the heart, liver and kidney of male adult Filipinos was determined and found to be agreeable with the normal mean values reported in literature. The mean concentration of zinc in the heart and liver of patients who died of myocardial infarction,  $28.85 \pm 2.07$  ug/g and  $37.57 \pm 8.38$  ug/g respectively were lower than the normal values of  $30.35 \pm 2.53$  ug/g and  $47.30 \pm 7.72$  ug/g. The mean level of copper in patients with

myocardial infarction of  $3.95 \pm 0.82$  ug/g was lower than the normal value of  $5.01 \pm 1.96$  ug/g. The mean concentration of molybdenum of  $0.83 \pm 0.13$  ug/g,  $0.76 \pm 0.36$  ug/g and  $0.74 \pm 0.31$  ug/g in the heart, liver and kidney respectively of patients with myocardial infarction were higher than the normal values of  $0.32 \pm 0.13$  ug/g,  $0.52 \pm 0.16$  ug/g and  $0.41 \pm 0.20$  ug/g.

The results and importance of our investigation was discussed.

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