CHAPTER III

OBSERVATIONS

OBSERVATIONS :

1) OBSERVATIONS DURING ACUTE TOXICITY TEST OF URANYL NITRATE :

In contrast to the control animals, uranyl nitrate (UN) induced animals manifested a definate behavioural change after the UN injection (5 mg/kg and 10 mg/kg). The general appearance of rats following UN intoxication varies according to dose and time, upto 24 hours animals looks normal however, they showed seldom, irritable movement. Within 24 to 48 hours animals became inactive, limp and responseless. They showed little interest in food and water. Rats treated with UN, 5 mg/kg, body wt. became moribund about 5 days after the treatment and mortality was maximum between 6 to 8 days, with a higher dose concentration of 10 mg/kg mortality was maximum between 4 to 6 days. Body weight of the control rat increase normally however, UN administered animal for the both dose concentrations showed a gradual loss in body weight, became moribund and died in coma.

A) Onset of early initiation phase (2 hrs, 4 hrs) of uranyl nitrate induced acute renal failure.

(i) Hematological observations :

The difference in hematological observations during early initiation phase (2 hrs, 4 hrs) of treatment with 5 mg/kg UN are exhibited in Table-1.

In early initiation phase there was a considerable retardation in the rate of coagulation as compared to the control one. The retardation was about 40 percent. The erythrocyte

TABLE - 1

HEMATOLOGICAL OBSERVATION DURING THE EARLY INITIATION PHASE (2, 4 hrs) OF URANYL NITRATE INDUCED ACUTE RENAL FAILURE.

Hours	Clotting time	E. S. R. mm		Hemoglobin	Total R.B.C.	Total W.B.C.	Differential Count (%)				
	minutes	I hr	II hr	gms/100 ml	$10^6/mm^3$	$10^3/mm^3$	Lymphocytes	Monocytes	Neutrophils	Basophils	Eosinophils
Control	2.3 ± 0.05	8 ± 0.17	7.5 ± 0.37	16.8 ± 1.01	7.4 ± 0.11	12 ± 0.20	65 ± 2.90	11 ± 1.94	19 ± 2.21	4 ± 0.97	1
2	2.5 ± 0.02 ***	8 ± 0.29 NS	7.8 ± 0.30 NS	13.5 ± 1.06 ***	6.1 ± 0.13 ***	7.8 ± 0.15 ***	68 ± 2.21 ***	9 ± 1.10 NS	10 ± 1.10 ***	10 ± 0.61 NS	3 ± 1.37
4	2.5 ± 0.09	9.1 ± 0.23 ***	8.9 ± 0.24 ***	13.4 ± 1.04 ***	6.4 ± 0.10 ***	6.06 ± 0.20 ***	72 ± 2.17 ***	8 ± 0.97	16 ± 1.65	2 ± 0.68	2 ± 0.97

Dose : 5 mg/kg body weight.

All values are mean ± SE of 5 animals.

P values :- *** = $P < 0.01$, NS = Not significant.

sedimentation rate was found to be accelerated in this phase during the I and II hour observation of E.S.R. (13-19 percent; $P < 0.01$). The hemoglobin concentration after the treatment with 5 mg/kg UN showed gradual decrease in this phase. The degrease was to the tune of 20 percent ($P < 0.01$; Fig.1). There was a gradual fall in the red blood cell number to the extent of 13-17 percent ($P < 0.01$) after the UN administration in this phase (Fig.2). White blood cells also exhibited decrease in number, however the decrease was to the tune of 30-35 percent ($P < 0.01$) as compared to the control animal (Fig.2). The differential count in this phase showed increase number of lymphocytes (10-15 percent $P < 0.01$). On the contrary monocytes and neutrophils showed a relative fall in their values after the treatment with UN. The basophils gave incosistant results in this phase of ARF and no definite rise in eosinophils number was observed.

The differences in hematological observations during early initiation phase (2 hrs, 4 hrs) of treatment with 10 mg/kg UN are exhibited in Table 2.

As compared to the sublethal dose of UN (5 mg/kg) the lethal dose of UN (10 mg/kg) exhibited relatively different results in this phase of ARF. The retardation in the clotting time at this dose concentration was found to be 15-55 percent (($P < 0.01$). The acceleration in erythrocyte sedimentation rate was to the tune of 6-13 percent. The hemoglobin concentration showed 10 percent decrease as compared to the control animal(Fig.1)

TABLE - 2

HEMATOLOGICAL OBSERVATIONS DURING THE EARLY INITIATION PHASE (2, 4 hrs) OF URANYL NITRATE INDUCED ACUTE RENAL FAILURE.

Hours	Clotting time	E. S. R. mm		Hemoglobin	Total R.B.C.	Total W.B.C.	Differential Count (%)				
	minutes	I hr	II hr	gms/100 ml	$10^6/mm^3$	$10^3/mm^3$	Lymphocytes	Monocytes	Neutrophils	Basophils	Eosinophils
Control	2.3 ± 0.05	8 ± 0.17	7.5 ± 0.37	16.8 ± 1.01	7.4 ± 0.20	12 ± 2.90	65 ± 2.90	11 ± 1.94	19 ± 2.21	4 ± 0.97	1
2	2.78 ± 0.05	8.6 ± 0.15 ***	8.4 ± 0.09 **	15.4 ± 0.18	6.18 ± 0.25 ***	7.44 ± 0.06 ***	70 ± 1.65	10 ± 1.10 ***	13 ± 1.37	5 ± 0.97 NS	2 ± 0.30
4	2.7 ± 0.05 ***	9 ± 0.13 ***	8 ± 0.15 NS	15.1 ± 0.36	6.4 ± 0.30 ***	8.86 ± 0.06 ***	69 ± 0.97	6 ± 1.10 ***	15 ± 2.40	7 ± 1.56	3 ± 0.92

Dose : 10 mg/kg, body weight.

All values are mean ± SE of 3 animals.

P values :- *** = $P < 0.01$; ** = $P < 0.05$; NS = Not significant.

(However, this decrease was relatively less than that of sublethal dose of 5 mg/kg UN). The red blood cell number was found to be decreased to 10-13 percent ($P < 0.01$, Fig.2). The white blood cell count showed 25-40 percent decrease in their percent values (Fig.3). The hemoglobin concentration, the total R.B.C., W.B.C. count however, showed less decrease in their values as compared to the sublethal dose of UN at this phase of ARF. The differential count exhibited again significant results at this dose concentration. Lymphocytes showed very little increase in their percent values (7 percent). However, monocytes and neutrophils showed about 50 percent increase in their percent values as compared to the control one. Basophils, at this dose concentration showed increase in their percent values to the tune of 25-75 percent. Eosinophils showed significant increase in their number.

II) Biochemical Observations :

The blood urea nitrogen at two different dose concentrations of UN in the early initiation phase of ARF is shown in Table-7.

In this phase, at both the dose concentrations (5 mg/kg, 10 mg/kg), the blood urea nitrogen was found to be increased significantly ($P < 0.05$, $P < 0.01$; Fig.4).

The level of tri-acyl-glycerol hydrolase activity during the early initiation phase of UN induced ARF (5 mg/kg and 10 mg/kg) is indicated in Table-8.

In this phase the tri-acyl-glycerol hydrolase activity

was found to be elevated to the tune of 50-90 percent after the administration of low dose of 5 mg/kg. On the other hand the lipolytic activity after high dose of 10 mg/kg; UN, showed only 5-50 percent elevation (Fig. 5).

B) Late initiation phase(4 hrs, 8 hrs) of uranyl nitrate induced acute renal failure.

I) Hematological observation :

The alterations in hematology after the sublethal dose of uranyl nitrate 5 mg/kg during the late initiation phase of ARF is given in Table-3.

During this phase of UN induced ARF there was a decrease in rate of clotting time of the animal (5-10 percent) however this decrease was significant as compared to the early initiation phase of the acute renal failure. The erythrocyte sedimentation rate was accelerated to 12-18 percent ($P < 0.01$). The hemoglobin concentration was decreased to the tune of 10-15 percent ($P < 0.01$), however this decrease was less as compared to the early initiation phase of ARF (Fig. 1). The total red blood cells decreased to about 10 percent ($P < 0.01$, Fig. 2) and white blood cells to about 50 percent ($P < 0.01$, Fig. 3). The differential count showed a little increase in lymphocyte number (5-10 percent). Monocytes increased suddenly in this phase to about 10-20 percent which were found to be decreased in the early initiation phase. Neutrophils showed again a decrease to about 5-30 percent; but it was less than early initiation phase. Basophils showed about 25 percent increase in this phase of ARF. However eosinophils showed no significant change.

TABLE - 3

HEMATOLOGICAL OBSERVATIONS DURING THE LATE INITIATION PHASE (8, 12 hrs) OF UN INDUCED ACUTE RENAL FAILURE.

Hours	Clotting time minutes	E. S. R. mm I hr	E. S. R. mm II hr	Hemoglobin gms/100 ml	Total R.B.C. $10^6/mm^3$	Total W.B.C. $10^3/mm^3$	Differential Count (%) Lymphocytes	Monocytes	Neutrophils	Basophils	Eosinophils
Control	2.3 ± 0.05	8 ± 0.17	7.5 ± 0.37	16.8 ± 1.01	7.4 ± 0.11	12 ± 0.20	65 ± 2.90	11 ± 1.94	19 ± 2.21	4 ± 0.97	1
8	2.50 ± 0.09	9 ± 0.26 ***	8.8 ± 0.13 ***	14.8 ± 1.19	6.7 ± 0.12 ***	7 ± 0.27 ***	68 ± 2.06	13 ± 1.53	12 ± 1.96 ***	4 ± 0.61 NS	3 ± 0.61
12	2.73 ± 0.06	9.3 ± 0.16 ***	8.8 ± 0.15 ***	14.4 ± 1.00 ***	6.8 ± 0.12 ***	6.2 ± 0.20 ***	71 ± 1.94 ***	12 ± 0.92 NS	9 ± 1.10 ***	5 ± 1.96 NS	3 ± 1.10

Dose : 5 mg/kg body weight.

All values are mean ± SE of 3 animals.

P values :- *** = $P < 0.01$, NS = Not significant.

After a lethal dose of uranyl nitrate 10 mg/kg) the hematological values altered significantly from that of early dose of 10 mg/kg UN. The values are as shown in Table-4.

The clotting time was retarded to the extent of 10-40 percent ($P < 0.01$) at this concentration and was significantly greater than the early dose of 5 mg/kg uranyl nitrate at this phase of ARF. The erythrocyte sedimentation rate also showed less acceleration as compared to the early dose of 5 mg/kg. The acceleration was about 5-10 percent ($P < 0.05$). The hemoglobin concentration decreased to 13-16 percent ($P < 0.01$, Fig.1). This decrease was higher than the decrease during the early dose of 5 mg/kg uranyl nitrate. The total number of red blood cells showed again a gradual fall at this dose concentration, (about, 18 percent, $P < 0.01$) however this decrease was higher as compared to the 5 mg/kg; UN (Fig.2). The white blood cell number was also decreased to 16-30 percent (Fig.3). The lymphocytes showed 7 percent increase and the monocytes showed 25-60 percent increase in their values. Neutrophils showed a decrease to the extent of 10-30 percent, while basophils showed a relative increase (25-125 percent) in this phase of ARF. Eosinophils gave insignificant results in this phase.

II) Biochemical Observations :

The blood urea nitrogen level during the late initiation phase of ARF at different dose concentrations (5 mg/kg and 10 mg/kg) is as shown in Table-7.

In this phase of acute renal failure the elevation in the

TABLE - 4

HEMATOLOGICAL OBSERVATIONS DURING THE LATE INITIATION PHASE (8, 12 hrs) OF URANYL NITRATE INDUCED ACUTE RENAL FAILURE.

Hours	Clotting time	E. S. R. mm		Hemoglobin	Total R.B.C.	Total W.B.C.	Differential Count (%)				
	minutes	I hr	II hr	gms/100 ml	$10^6/mm^3$	$10^3/mm^3$	Lymphocytes	Monocytes	Neutrophils	Basophils	Eosinophils
Control	2.3 ± 0.05	8 ± 0.17	7.5 ± 0.37	16.8 ± 1.01	7.4 ± 0.11	12 ± 0.20	65 ± 2.90	11 ± 1.94	19 ± 2.21	4 ± 0.97	1
8	2.95 ± 0.04 ***	8.2 ± 0.12 **	8.5 ± 0.17 **	14.5 ± 0.22	6.1 ± 0.02 ***	7.74 ± 0.09 ***	62 ± 0.68	14 ± 1.94 ***	18 ± 1.56	5 ± 0.61 NS	1
12	2.90 ± 0.05 ***	9 ± 0.11 ***	8.5 ± 0.16 **	14.0 ± 0.20	6.0 ± 0.09 ***	10.94 ± 0.12 ***	65 ± 1.56 **	15 ± 1.65 ***	13 ± 2.17 **	5 ± 0.18 **	2 ± 0.61

Dose : 10 mg/kg, body weight.

All values are mean ± SE of 3 animals.

P values :- *** = $P < 0.01$; ** = $P < 0.05$; NS = Not significant.

level of blood urea nitrogen was persistent. The BUN after a dose of 5 mg/kg showed about 35-50 percent ($P < 0.01$) increase. On the other hand, after a high dose of 10 mg/kg BUN was elevated to 65-80 percent ($P < 0.01$, Fig. 4).

The level of tri-acyl-glycerol hydrolase activity during the late initiation phase of acute renal failure after two different doses of uranyl nitrate (5 mg/kg and 10 mg/kg) is as shown in Table-8.

In the late initiation phase after a sublethal dose of 5 mg/kg UN lipolytic activity showed a gradual elevation. The elevation was to the tune of 105-129 percent ($P < 0.01$) as compared to the control animal. While under the effect of high dose of UN (10 mg/kg) the elevation in the lipolytic activity was 130-150 percent. At both the dose concentration the elevation in the lipolytic activity was persistant (Fig. 5).

C) Maintainance phase (48 hrs, 72 hrs) of uranyl nitrate induced acute renal failure.

I) Hematological observations :

The hematological alterations during the maintenance phase of ARF induced by 5 mg/kg dose of uranyl nitrate are as shown in Table-5.

As the late initiation phase (12 hrs, 24 hrs) progressed into fully developed maintenance phase hematological observations manifested significant results as compared to the control animals. The retardation of clotting time reached to the extent of 13 %

TABLE - 5

HEMATOLOGICAL OBSERVATION DURING THE MAINTENANCE PHASE (48, 72 hrs) OF URANYL NITRATE INDUCED ACUTE RENAL FAILURE.

Hours	Clotting time minutes	E. S. R. mm I hr	E. S. R. mm II hr	Hemoglobin gms/100 ml	Total R.B.C. $10^6/mm^3$	Total W.B.C. $10^3/mm^3$	Differential Count (%) Lymphocytes	Monocytes	Neutrophils	Basophils	Eosinophils
Control	2.3 ± 0.05	8 ± 0.17	7.5 ± 0.37	16.8 ± 1.01	7.4 ± 0.11	12 ± 0.20	65 ± 2.90	11 ± 1.94	19 ± 2.21	4 ± 0.97	1
48	3.20 ± 0.05	9.2 ± 0.19 ***	8.9 ± 0.15 ***	14.0 ± 1.04 ***	6.63 ± 0.12 ***	5 ± 0.25 ***	68 ± 1.22	13 ± 1.65	11 ± 2.40 ***	4 ± 1.10 NS	4 ± 0.61
72	3.45 ± 0.04	8.7 ± 0.26 ***	8.5 ± 0.16 **	14.2 ± 1.01 ***	6.40 ± 0.06 ***	5.3 ± 0.19 ***	69 ± 0.97	12 ± 2.06 NS	13 ± 1.10	3 ± 0.97 ***	3 ± 0.30

Dose :- 5 mg/kg, body weight.
All values are mean ± SE of 3 animals.
P values :- *** = $P < 0.01$; ** = $P < 0.05$; NS = Not significant.

under the effect of 5 mg/kg uranyl nitrate. At this dose concentration erythrocyte sedimentation rate was accelerated to 10-20 percent ($P < 0.01$). The hemoglobin concentration showed a subsequent decrease to the tune of 15 percent ($P < 0.01$; Fig.1). While red blood cells showed a relative decrease to 10-13 percent under the toxic effect of uranyl nitrate 5 mg/kg (Fig.2). White blood cells showed a persistant state of gradual decrease in their percent values, the decrease was found to be 60 percent in this phase of ARF (Fig.3). The lymphocytes showed about 5 percent increase, while monocytes showed 10-20 percent increase in their percent values. Neutrophils showed about 30-40 percent decrease. Basophils gave no significant alteration in their percent values, on the contrary eosinophil number was increased to a considerable extent.

The hematological alterations under the effect of 10 mg/kg uranyl nitrate in the maintenance phase of ARF is exhibited in Table-6.

At this dose concentration, the rate of coagulation was affected significantly and retarded to 35-60 percent ($P < 0.01$) in this phase. The erythrocyte sedimentation rate was accelerated to about 10-15 percent ($P < 0.01$). The hemoglobin concentration reduced to 20 percent in this phase (Fig.1). The red blood cells decreased about 25 percent ($P < 0.01$, Fig.2). The total white blood cell count showed a maximum decrease in their percent value (30-45 percent, $P < 0.01$) as compared to earlier phase (Fig.3). The differential count gave significant results in this phase. Lymphocytes and monocytes showed a subsequent

TABLE - 6

HEMATOLOGICAL OBSERVATIONS DURING THE MAINTENANCE PHASE (48, 72 hrs) OF URANYL NITRATE INDUCED ACUTE RENAL FAILURE.

Hours	Clotting time minutes	E. S. R. mm I hr	E. S. R. mm II hr	Hemoglobin gms/100 ml	Total R. B. C. $10^6/mm^3$	Total W. B. C. $10^3/mm^3$	Differential Count (%) Lymphocytes	Monocytes	Neutrophils	Basophils	Eosinophils
Control	2.3 ± 0.05	8 ± 0.17	7.5 ± 0.37	16.8 ± 1.01	7.4 ± 0.11	12 ± 0.20	65 ± 2.90	11 ± 1.94	19 ± 2.21	4 ± 0.97	1
48	3.45 ± 0.04 ***	9 ± 2.64 ***	8.6 ± 0.23 ***	13.6 ± 0.24	5.68 ± 0.21 ***	7.8 ± 0.12 ***	72 ± 2.17 ***	12 ± 0.91 NS	8 ± 1.26 ***	6 ± 0.92	2 ± 0.30
72	3.50 ± 0.04 ***	9.6 ± 0.06 ***	8 ± 0.19 NS	13 ± 0.18	5.40 ± 0.03 ***	6.84 ± 0.01 ***	72 ± 2.45 **	12 ± 0.61 NS	6 ± 1.87 ***	9 ± 0.97 ***	1

Dose :- 10 mg/kg, body weight.

All values are mean ± SE of 3 animals.

P values :- *** = $P < 0.01$; ** = $P < 0.05$; NS = Not significant.

increase to about 10 percent. The neutrophils showed maximum decrease in this phase (60-70 percent, $P < 0.01$), on the contrary basophils showed a maximum increase in this phase (50-125 percent). Eosinophils gave no significant result.

II) Biochemical observations :

The effect of uranyl nitrate (5 mg/kg and 10 mg/kg) on the blood urea nitrogen in the maintenance phase of ARF is expressed in Table-7.

The blood urea nitrogen under the effect of 5 mg/kg UN showed a maximum elevation in their values (Fig.4); the increase was to the extent of 70-85 percent ($P < 0.01$), on the contrary at the higher dose concentration (10 mg/kg), the BUN was found to be elevated to 95-175 percent ($P < 0.01$) in the maintenance phase of ARF.

The level of tri acyl glycerol hydrolase activity in the maintenance phase of ARF under two different dose concentrations of UN (5 mg/kg and 10 mg/kg) is expressed in the Table-8.

At the lower dose concentration of 5 mg/kg uranyl nitrate the elevation in the lipolytic activity was persistant (20-40 percent, $P < 0.01$). However, there was considerable fall in the elevation in this phase as compared to the late initiation phase. After the administration of 10 mg/kg UN the lipolytic activity showed a significant elevation to the tune of 90-105 percent ($P < 0.01$) however this elevation was also less than that of late initiation phase. The relative elevation in the tri acyl glycerol hydrolase activity in the maintenance phase of ARF

TABLE - 7

EFFECT ON BLOOD UREA NITROGEN LEVEL AFTER THE ADMINISTRATION OF URANYL NITRATE.

Hours	Dose : 5 mg/kg; body wt. BUN (mg/100 ml)	Dose : 10 mg/kg body wt. BUN (mg/100 ml)
Control	20 ± 0.3437	20 ± 0.3437
2	21 ± 1.5371	22 ± 1.1084
4	23.5 ± 1.2005 **	28 ± 1.7926 ***
8	27 ± 2.0908	33.5 ± 1.1706
12	30.5 ± 0.6337 ***	37 ± 0.7838 ***
48	34 ± 0.7685 ***	39 ± 1.2005 ***
72	36 ± 1.3223 ***	43 ± 1.2393 ***

All values are mean ± SE of 3 animals.

P values :- *** = $P < 0.01$; ** = $p < 0.05$.

TABLE - 8

LEVEL OF SERUM TRI ACYL GLYCEROL HYDROLASE ACTIVITY DURING DIFFERENT PHASES OF URANYL NITRATE INDUCED ACUTE RENAL FAILURE.

Hours	Lipase Unit/gms Dose - 5 mg/kg	Lipase Unit/gms. Dose - 10 mg/kg.
Control	3.4 ± 0.1108	3.4 ± 0.1108
2	5.0 ± 0.1374 ***	3.6 ± 0.1537
4	6.6 ± 0.1655 ***	5.2 ± 0.1792 ***
8	7.8 ± 0.1944 ***	8.4 ± 0.2062 ***
12	7 ± 0.0972 ***	7.8 ± 0.2916 ***
48	5.0 ± 0.1267 ***	7.0 ± 0.2341 ***
72	4.2 ± 0.1567 ***	6.6 ± 0.2626 ***

All values are mean ± SE of 3 animals.

P value :- *** = $p < 0.01$.

induced by uranyl nitrate (5 mg/kg and 10 mg/kg) is depicted in Fig.5.

The alterations in the hematological values after 5 mg/kg dose of UN administration in rat, in various phases of acute renal failure is expressed in Table-9.

The packed cell volume (PCV) showed a definite rise in their percent values (about 7 percent) after the UN administration, this rise was consistant throughout the different phases of ARF. The mean corouscular volume (MCV) showed a gradual increase in their values (10-20 percent) as the pathogenic condition progresses during acute renal failure. The mean corpuscular hemoglobin (MCH) showed a progressive loss in their percent values (7-15 percent) throughout the various phases of acute renal failure. The mean corpuscular hemoglobin concentration also showed a significant fall in their percent values (20-30 percent) during the progression of acute renal failure as compared to the control values. At this dose concentration colour index was found to be below one in all phases of UN induced ARF.

The comparative hematological values after the dose of 10 mg/kg uranyl nitrate during the various phases of acute renal failure are shown in Table-10.

From Table-10, it can be seen that under the effect of higher dose of uranyl nitrate (10 mg/kg), there was a significant change in the hematological values of the animal. The PCV percent values showed a sudden increase in their values. In the

TABLE - 9

ALTERATIONS IN THE HEMATOLOGICAL VALUES AFTER THE URANYL NITRATE (5 mg/kg, body wt.) ADMINISTRATION IN RAT.

Blood values	Control	Hours					
		2	4	8	12	48	72
PCV (%)	65.0	70	64	68	70	70	70
MCV (μm^3)	87.80	114.7	100	101.4	102.9	105.5	109.5
MCH (Pg)	24	22.13	20.93	20.84	21.17	21.1	22.1
MCHC (gHb/100 ml/RBC)	27.33	19.2	20.9	20.5	21.1	20.0	20.2

TABLE - 10

ALTERATIONS IN THE HEMATOLOGICAL VALUES AFTER URANYL NITRATE (10 mg/kg, body wt.) ADMINISTRATION IN RAT.

Blood values	Control	HOURS					
		2	4	8	12	48	72
PCV (%)	65.0	70	67	68	65	67	68
MCV (μm^3)	87.8	106	104.6	111.4	108.3	117.9	125.9
MCH (Pg)	24	23.3	23.5	23.7	23.3	23.9	24
MCHC (gHb/100 ml/RBC)	27.33	21.98	22.4	21.2	21.5	20.2	19.0

first two phases of ARF (5-7 percent), on the contrary in the maintenance phase, the increase was only 3 percent. The MCV values showed 20 percent increase in early initiation phase, 25 percent increase in late initiation phase and 30-40 percent rise in maintenance phase of ARF at this dose concentration. However, these values showed significant rise as compared to the earlier low dose of 5 mg/kg UN. The MCH showed a definite fall in their percent values, however, at this dose concentration fall in the percent value was less as compared to the earlier dose of 5 mg/kg UN. The MCHC showed about 20 percent decrease in the early initiation phase and late initiation phase of the ARF. On the other hand it decreased to the extent of 30 percent in the maintenance phase of ARF. The colour index at this dose concentration was above one.

OBSERVATION DURING PROLONGED TOXICITY TEST OF URANYL NITRATE :

For the prolonged toxicity test three different dose concentrations, such as 0.2, 0.5 and 1 mg/kg, body weight were used. These doses were given every alternate day and hematological and biochemical observations were made after 31 days.

I) Hematological observations :

The hematological observations during the prolonged toxicity test of uranyl nitrate (0.2, 0.5 and 1 mg/kg) are expressed in Table-11.

The hematological observation during prolonged toxicity test under different concentrations of UN gave significant results. As can be seen from Table-11, the clotting time

TABLE - 11

HEMATOLOGICAL OBSERVATIONS DURING PROLONGED TOXICITY TESTS OF URANYL NITRATE.

Dose mg/kg body wt.	Days	Clotting time minutes	E. S. R. mm I hr	E. S. R. mm II hr	Hemoglobin gms/100 ml	Total R.B.C. $10^6/mm^3$	Total W.B.C. $10^3/mm^3$	Differential Count (%) Lymphocytes	Monocytes	Neutrophils	Basophils	Eosinophils
Control	-	2.3 ± 0.05	8 ± 0.17	7.5 ± 0.37	15.8 ± 1.01	7.4 ± 0.31	12 ± 0.20	65 ± 2.90	11 ± 2.90	19 ± 2.21	4 ± 1.65	1
0.2	31	2.3 ± 0.03	9.8 ± 0.06 ***	8.9 ± 0.24 ***	14 ± 0.16 **	6.06 ± 0.01 ***	6.5 ± 0.01 ***	72 ± 0.97 **	12 ± 0.92	8 ± 0.61 ***	6 ± 0.97	2 ± 0.30
0.5	31	2·60 ± 0.04 *	9.5 ± 0.13 ***	9.1 ± 0.23 ***	14 ± 0.33 ***	6.1 ± 0.03 ***	8.3 ± 0.09 ***	78 ± 1.37 ***	8 ± 0.30	8 ± 1.26 ***	4 ± 0.61	2 ± 0.61
1	31	2·60 ± 0.01 *	9.9 ± 0.03 ***	9.3 ± 0.16 ***	12.5 ± 0.17 **	5.85 ± 0.02 ***	9.8 ± 0.03 ***	72 ± 0.68 **	20 ± 1.22 ***	6 ± 0.68 ***	1	1

All values are mean ± SE of 3 animals.

P values :- *** = $P < 0.01$; ** = $P < 0.05$; * = $P < 0.1$; NS = Not significant.

retarded to about 13 percent in the animal treated with 0.5 and 0.1 mg/kg uranyl nitrate, however, 0.2 mg/kg uranyl nitrate dose concentration could not alter the clotting time. The erythrocyte sedimentation rate was considerably accelerated by the effect of all the three dose concentrations of uranyl nitrate, the 0.2 mg/kg dose concentration of uranyl nitrate accelerated ESR, 18-20 percent ($P < 0.01$); while 1 mg/kg dose concentration of UN accelerated ESR to about 25 percent ($P < 0.01$). The hemoglobin concentration was brought down to about 16 percent ($P < 0.01$, < 0.5) for the first two doses (0.2, 0.5 mg/kg, UN); On the other hand 1 mg/kg dose of UN reduced hemoglobin concentration to about 25 percent ($P < 0.05$). The prolonged toxic effect of different concentrations of UN on total red blood cell count showed subsequent decrease in their percent values (18-20 percent, $P < 0.01$). The 0.2 ml/kg and 0.5 mg/kg dose concentration of uranyl nitrate affected the white blood cell total count considerably. There was a subsequent 30-45 percent ($P < 0.01$), loss in the total white blood cell count, while 1 mg/kg dose of UN could reduce the total white blood cell count to an extent of 18 percent only ($P < 0.01$). In the differential count lymphocytes showed about 10-20 percent ($P < 0.05$, $P < 0.01$) rise in their percent values for different dose concentrations of the uranyl nitrate. Monocyte number was greatly enhanced to 80 percent by 1 mg/kg dose of uranyl nitrate, however, earlier dose gave incosistant results. Neutrophil number was enhanced to a considerable extent (60-70 percent, $P < 0.01$). Basophils and eosinophils however give insignificant result for the prolonged toxicity test.

The alteration in hematological values after the prolonged toxicity of uranyl nitrate administered with three different doses are expressed in Table-12.

The packed cell volume (PCV) increased to about 10-20 percent. The mean corpuscular volume (MCV) showed a definite rise for three different dose concentration of uranyl nitrate (30-50 percent). The mean corpuscular hemoglobin (MCH) reduced to 3-11 percent after a prolonged exposure of different concentration of uranyl nitrate. While mean corpuscular hemoglobin concentration (MCHC) reduced to 25-35 percent after the different doses of uranyl nitrate for prolonged administration. Colour index was found to be above one.

II) Biochemical results :

The prolonged effect of uranyl nitrate (0.2, 0.5 and 1 mg/kg) on blood urea nitrogen level is expressed in Table-13.

The blood urea nitrogen after the three different doses of uranyl nitrate exhibited only 10-15 percent ($P < 0.05$) increase.

The tri-acyl-glycerol hydrolase activity after the prolonged effect of uranyl nitrate (0.2, 0.5 and 1 mg/kg) is as shown in Table-14.

The animals under the prolonged administration of 0.2 mg/kg dose of UN showed about 5 percent enhancement in the lipolytic activity and this activity goes on increasing gradually as the dose concentration increases. For the dose of 0.5 mg/kg UN there was substantial 10 percent elevation on the other hand the higher

dose of 1 mg/kg UN gave maximum enhancement to the tune of 15 percent in the serum lipolytic activity of the animal.

TABLE - 12

ALTERATIONS IN HEMATOLOGICAL VALUES AFTER THE PROLONGED TREATMENT OF URANYL NITRATE.

Blood values	Control	Dose (mg/kg)		
		0.2	0.5	1
PCV (%)	65	72	78	70
MCV ($/um^3$)	87.8	113	127.8	119.6
MCH (Pg)	24	23.10	22.9	21.36
MCHC (gHb/100 ml/RBC)	27.33	20.33	17.9	17.8

TABLE - 13

EFFECT ON BLOOD UREA NITROGEN LEVEL IN PROLONGED TOXICITY TEST OF URANYL NITRATE.

Dose mg/kg, body wt.	BUN (mg/100 ml)
Control	20 ± 0.8278
0.2	22 ± 1.1084 **
0.5	22 ± 1.2393 **
1	23 ± 1.3749 **

All values are mean ± SE of 3 animals.

P values :- ** = $p < 0.05$.

TABLE - 14

LEVEL OF SERUM TRI ACYL GLYCEROL HYDROLASE ACTIVITY DURING PROLONGED TOXICITY TEST OF URANY NITRATE.

Dose mg/kg; body wt.	Lipase units/gms.
Control	3.40 ± 0.1108
0.2	3.6 ± 0.1650 ***
0.5	3.75 ± 0.0179 ***
1	3.89 ± 0.136 ***

All values are mean ± SE of 3 animals.

P values :- *** = $p < 0.01$

CAPTION TO FIGURE 1

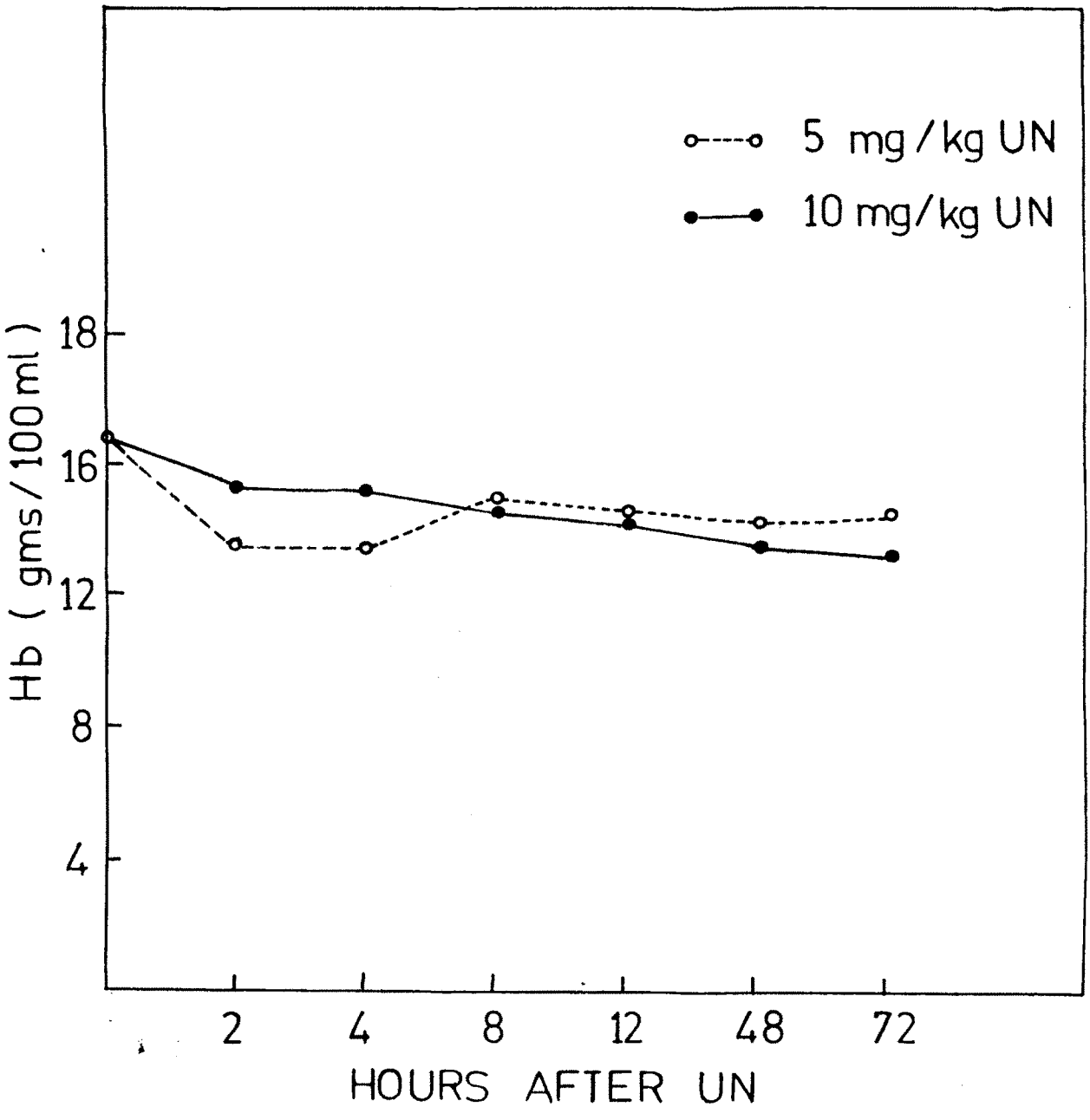
Figure showing influence of uranyl nitrate (o---o 5 mg/kg and • - • 10 mg/kg) on hemoglobin concentration of the experimental animal in different phases of UN toxicity.

2, 4 hrs - Early Initiation phase of UN toxicity,

8, 12 hrs - Late Initiation phase of UN toxicity,

48, 72 hrs - Maintenance phase of UN toxicity.

FIG-1


5 mg / kg UN
10 mg / kg UN
Hb (gms / 100 ml)
18
16
12
8
4
2
4
8
12
48
72
HOURS AFTER UN

CAPTION TO FIGURE 2

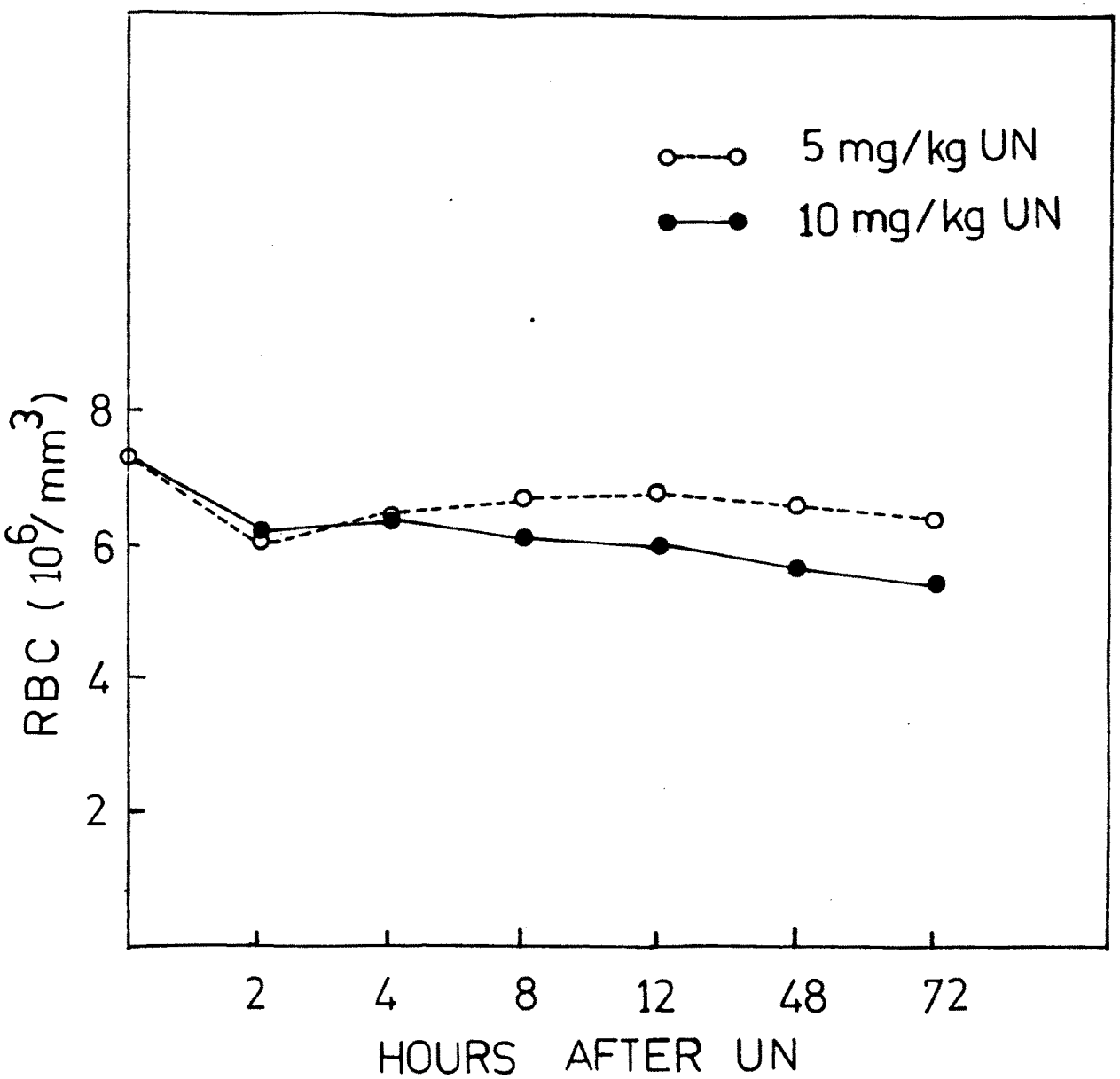
Graph showing influence of uranyl nitrate (O--O5 mg/kg and • - • 10 mg/kg) on total RBC mass of the experimental animal in different phases of UN toxicity.

2, 4 hrs - Early initiation phase of UN toxicity,

8, 12 hrs - Late initiation phase of UN toxicity,

48, 72 hrs - Maintenance phase of UN toxicity.

FIG-2



CAPTION TO FIGURE 3

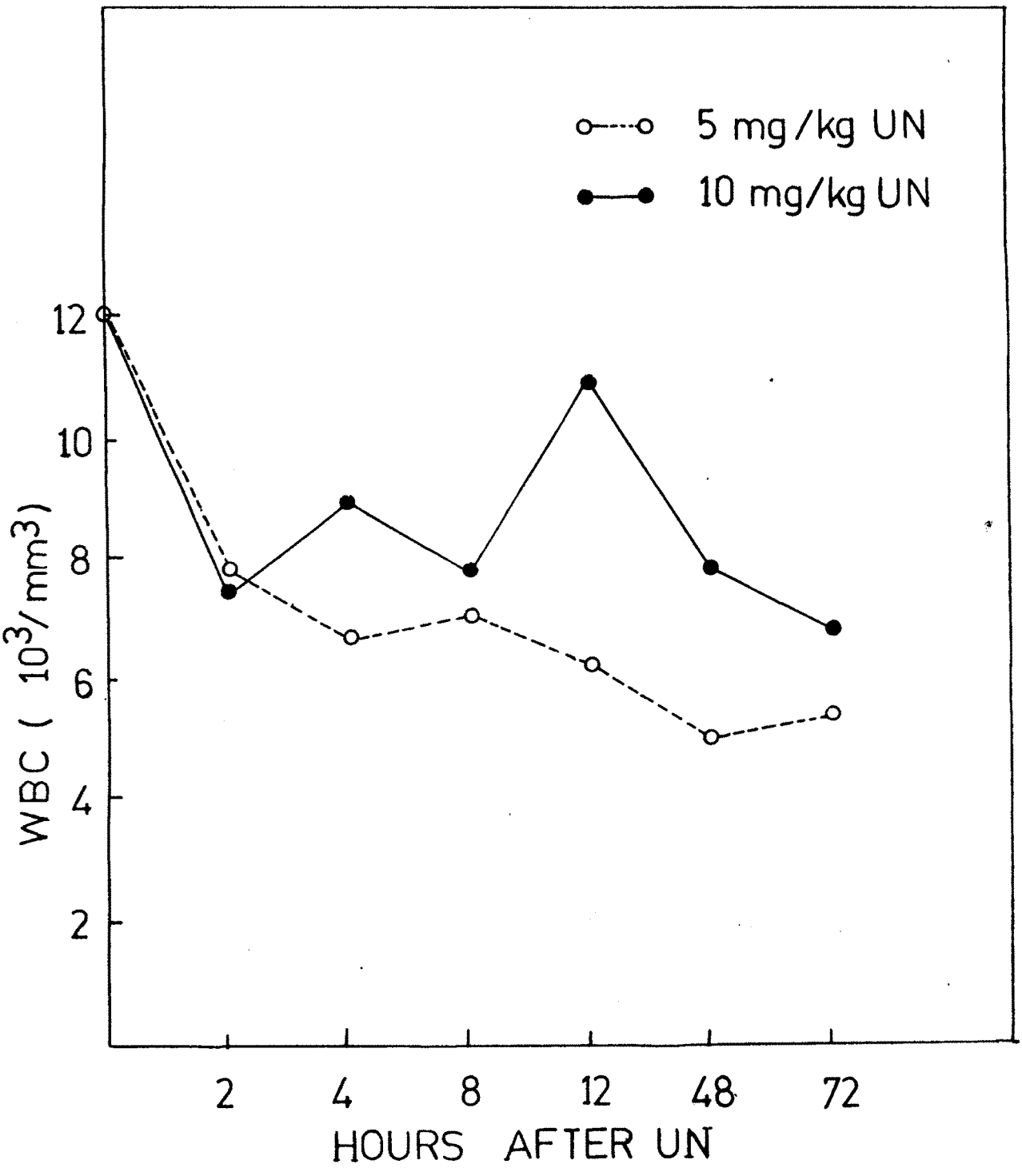
Graph showing influence of uranyl nitrate (o--o 5 mg/kg and • - • 10 mg/kg) on total WBC count of the experimental animal in different phases of UN toxicity.

2, 4 hrs - Early initiation phase of UN toxicity,

8, 12 hrs - Late initiation phase of UN toxicity,

48, 72 hrs - Maintenance phase of UN toxicity.

FIG-3


5 mg/kg UN
10 mg/kg UN
12
10
8
6
4
2
WBC (10^3/mm^3)
2
4
8
12
48
72
HOURS AFTER UN

CAPTION TO FIGURE 4

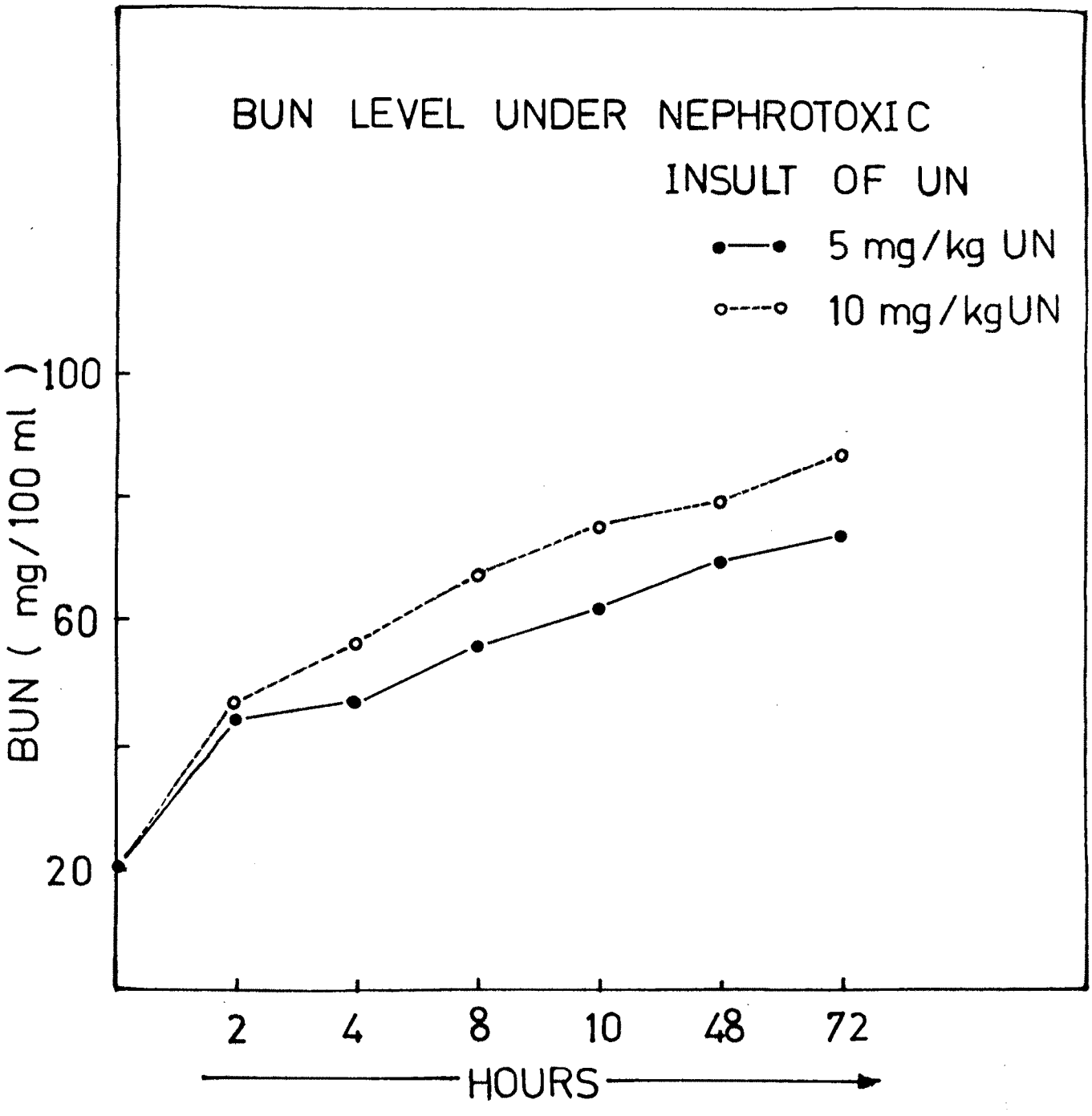
Level of Blood Urea Nitrogen (BUN) under the influence of uranyl nitrate (●---● 5 mg/kg, o _ o 10 mg/kg) during various phases of UN toxicity.

2, 4 hrs - Early initiation phase of UN toxicity,

8, 12 hrs - Late initiation phase of UN toxicity,

48, 72 hrs - Maintenance phase of UN toxicity.

FIG - 4


BUN LEVEL UNDER NEPHROTOXIC INSULT OF UN
5 mg/kg UN
10 mg/kgUN
BUN (mg/100 ml)
100
60
20
2
4
8
10
48
72
HOURS

CAPTION TO FIGURE 5

A Gross level of serum tri acyl glycerol hydrolase (TAGH) activity in rat, administered with two different dose concentrations of uranyl nitrate (5 mg/kg and 10 mg/kg). Lipolytic activity is expressed in units of free fatty acids released per ml serum.

2, 4 hrs - Early initiation phase of UN toxicity,

8, 12 hrs - Late initiation phase of UN toxicity,

48, 72 hrs - Maintenance phase of UN toxicity.

FIG-5