Protection from body weight loss by 2-mercaptopropionylglycine (MPG) in growing mice irradiated in utero with gamma radiation[1]

P.K. Dev, S.M. Gupta, P.K. Goyal, G. Mehta and B.P. Pareek

Radioembryology Group of the Radiation Biology Laboratory, Department of Zoology, University of Rajasthan, Jaipur-302004 (India), 2 June 1981

Summary. 2-Mercaptopropionylglycine administered during fetal growth period, protected significantly young mice against loss of body weight during postnatal development induced by 50 R gamma irradiation.

The radiosensitivity of the fetus has been extensively investigated in terms of developmental abnormalities and lethality[2-5]. 2-Mercaptopropionylglycine (MPG) has been shown to be radioprotective, and to be effective at a very low optimum dose, 20 mg/kg b.wt[6]. Studies on the chemical protection of the fetus against irradiation have received little attention[7-9]. We have shown earlier that the 2nd phase of weight loss in developing mice was averted by MPG[10,11]. The present paper deals with the protection of MPG against the effects of low doses of gamma radiation on the postnatal growth of mice irradiated in utero.

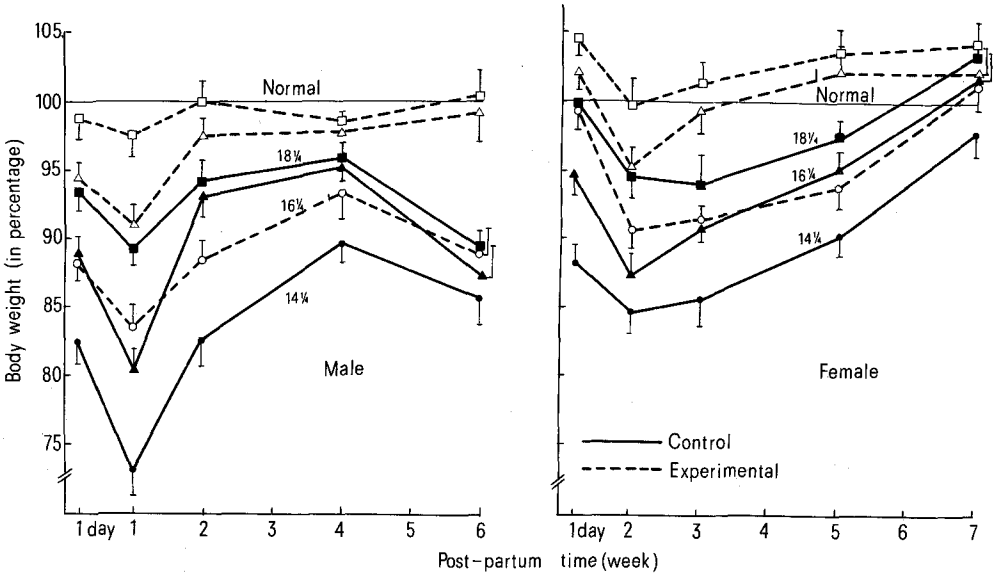
Materials and methods. Animals used in this investigation were taken from an inbred colony of Swiss albino mice maintained on rat/mice feed and water ad libitum. All mice were considered to have mated during the same time, i.e. after midnight, and pregnant females were irradiated in the morning at 09.00 h so that the embryological age at the time of irradiation on the 14th, 16th and 18th day after mating corresponded approximately to gestation days 14.25, 16.25 and 18.25. Females were divided into 2 groups each containing at least 7 animals from each gestation. The experimental group was injected i.p. with 20 mg/kg b.wt MPG (dissolved in double-distilled water with pH maintained at 6.4 with the addition of 0.1 N NaOH solution) 15-30 min before irradiation; while the control group received double-distilled water in a similar way. Animals of both the groups were exposed to 50R ^{60}Co whole-body gamma radiation at the dose rate of 50R/min. They were allowed to breed and the weight of the males and females of the litters was recorded separately at postnatal weekly intervals from day 1 to week 6 in the morning (table). The weight of normal colony animals of the same age was taken for comparison.

Results. The results were expressed in percent values, taking the normal weight as 100%, and are presented in the figure. In the control group, male offspring showed a bisphasic decline in weight - once at 1 week and again after 4 weeks - while female offspring after an initial weight loss at 1 week showed a continuous recovery to reach normal level at 6 weeks. In the experimental group, the initial weight loss was not readily apparent in the male and female offspring and the 2nd weight loss was completely prevented in the male offspring, except in those born to day 14.25 postconception irradiated mothers.

Discussion. From the results it appears that the male fetus is more prone to radiation damage during postnatal development. The effects of radiation on the postnatal growth of young ones exposed in utero, have been reported by a number of researches[12-14]. The present findings indicated that post-conception day 14.25 was particularly radiosensitive, and that the sensitivity decreased with the increase in fetal age. Nash and Gowen[13] showed that postnatal growth as measured by weight changes following irradiation in utero, was dependent on both the levels of irradiation and the embryological age at the time of irradiation.

The initial phase of weight loss of the newly born may be due to the direct effect of irradiation. Gupta et al.[9] suggested that weight loss in offspring was due to the highly suppressed thyroid function of the mother irradiated with ^{131}I during pregnancy.

The 2nd phase of weight decline in the males after a period of recovery may be due to growth retardation in later life. In the recovery phase, the cells which are not affected initially, grow and divide and are responsible for further increase in body weight. Other cells, however, which are not killed initially, later become abnormal or cease to divide and may result in the 2nd phase of weight loss. Such a biphasic mode of weight loss in both the male and female offspring of mice has been observed after relatively higher doses of gamma radiation were administered[10,11]. The ab-



Percent body weight changes during postnatal development in mice, irradiated with 50 R gamma rays in utero in presence or absence of MPG.

Showing number of gestating mice irradiated with 50 R gamma radiation in presence or absence of MPG and average litter size born

Day of irradiation (postconception)	Mode of treatment	No. of animals used	No. of young born	Average litter size	Young ones born (%) Male	Female	Mortality after birth (%)
	Normal	52	448	8.6	54.0	46.0	4.0
14.25	Control (irradiation)	10	88	8.8	48.8	51.2	2.0
	Experimental (irradiation + MPG)	8	70	8.7	52.8	47.2	Nil
16.25	Control	7	56	8.0	55.4	44.6	Nil
	Experimental	9	77	8.5	51.9	48.1	2.0
18.25	Control	12	96	8.0	47.9	52.1	Nil
	Experimental	8	67	8.3	54.0	46.0	Nil

sence of a 2nd phase of weight loss in female offspring may be due to the low dose used in this case. Females are reported to be less sensitive to radiation than males[15].

The chemical protector, cysteamine has been reported to protect the mouse fetus against irradiation[7]. MPG protected significantly the young ones against body weight loss after exposure to higher doses and also averted a 2nd phase of weight loss[10,11]. In the present study, animals in the experimental group (MPG treated) showed less weight reduction in the early intervals and almost complete recovery after 2 weeks. It appears that MPG arrested the mitotic activity of the cells[16] by reducing the mitotic-linked cell death, and protected against the initial weight loss. The increase in rate of mitotic activity following an initial stress in protected offspring may explain the absence of a 2nd weight loss due to the dose used in the present experiment.

1 Acknowledgment. The work was supported by a grant from CSIR, New Delhi, to P.K.D. which is gratefully acknowledged. The authors are also thankful to Prof. P. Navlakha for the irradiation facilities.

2 J.G. Wilson and J.W. Karr, Am. J. Anat. *88*, 1 (1951).
3 L.B. Russell, in: Radiation biology, vol. 1, p. 861. Ed. A. Hollaender. McGraw Hill, New York 1954.
4 R.L. Brent, Clin. Obstet. Gynec. *3*, 928 (1960).
5 R. Rugh and M. Wohlformm, Radiat. Res. *26*, 493 (1965).
6 T. Sugahara, Y. Tanaka, H. Nagata, T. Tanaka and E. Kano, in: Proceeding of the International Symposium on Thiola, p. 267. Santan Pharmaceutical, Osaka 1970.
7 R. Rugh and H. Clugston, Science *123*, 28 (1956).
8 J.M. Roberts, Teratology *3*, 319 (1970).
9 S.M. Gupta, P.K. Goyal and P.K. Dev, Experientia *37*, 888 (1981).
10 P.K. Dev, S.M. Gupta, P.K. Goyal, B.P. Pareek and G. Mehta, Strahlentherapie *157*, 553 (1981).
11 P.K. Dev, B.P. Pareek, S.M. Gupta, P.K. Goyal and G. Mehta, Acta anat. *112*, 249 (1982).
12 L.B. Russell, S.K. Badgett and C.L. Saylors, Int. J. Radiat. Biol., suppl. 343 (1959).
13 D.J. Nash and J.W. Gowen, Biol. Bull. *122*, 115 (1962).
14 P.G. Martin and R.L. Murphree, Radiat. Res. *40*, 330 (1969).
15 R. Rugh and J. Wolff, Proc. Soc. exp. Biol. Med. *92*, 408 (1956).
16 M.R. Saini and G.C. Jagetia, The protective effect of MPG on mammalian spleen after irradiation. To be presented at: 3rd World Federation of Nuclear Medicine and Biology. August 29–September 2, Paris 1982.

Normal immunosuppressive protein: inhibitory effect on hemagglutinin and plaque formation as well as B cell transformation by Epstein-Barr virus

D. Nelken and H. Ovadia

Laboratory of Immunohematology and Department of Immunology, Hadassah-Hebrew University Medical Center, P.O. Box 12000, Jerusalem 91120 (Israel), 20 November 1981

Summary. Injections of normal immunosuppressive protein (Nip) cause a significant decrease of hemagglutinin formation and plaque formation in rats immunized with sheep red blood cells. Nip added in vitro to human unbilical cord lymphocytes inhibits the B cell transformation caused by Epstein-Barr virus.

The immune reactivity is the result of a delicate balance between the stimulatory activity and the inhibitory activity triggered by the antigen. The modulation of this process is at present only partially understood. For several decades the enhancing part of the immune reaction has been widely studied and extensive knowledge has been accumulated, but the importance of suppressor factors and suppressor cells has been realized only in the last decade and our knowledge in this area is less extensive.

One of the suppressive factors that has been extensively studied in our laboratory is normal immunosuppresive protein (Nip)[2]. It is isolated from human blood or amniotic fluid[3]. By elution experiments with mannose from concavalin A-sepharose columns it has been shown to be a glycoprotein or glycopeptide, which is resistant to boiling and shows a positive PAS staining reaction[4].

The molecular weight of Nip, as determined by SDS polyacrylamide gel electrophoresis on the one hand and inability to leak through dialysis membranes with pore size of less than 10,000 on the other is about 15,000 daltons. It suppresses all lymphocyte activity whether expressed as B cell activity or T cell activity[5]. It also inhibits NK cell activity[6] and prevents the generation of suppressor cells[7]. At the same time Nip has no effect on macrophages or myeloid cells[8]. The binding of Nip to lymphocytes is reversible. It prevents DNA and RNA synthesis in the lymphocytes, is not toxic to the cells, and when it is washed away the cells regain their ability to carry out DNA and RNA synthesis after an interval for regeneration is allowed[3]. Nip is not species specific and the material prepared either from human plasma or human amniotic fluid shows similar suppressive activity on both human and