8. S. H. Cheng, S. Malcolm, S. Pemble, and B. Winchester, Biochem. J., 233, 65 (1986).
9. M. A. Chester, A. Lindblad, P.-A. Ockerman, and S. Autio, Genetic Errors of Glycoprotein Metabolism, ed. by P. Durand and J. O'Brien, Berlin (1982), pp. 89-122.
10. N. Dewji, N. Rapson, M. Greaves, and R. Ellis, Leukemia Res., 5, 19 (1981).
11. D. V. Marincovic and J. N. Marincovic, Biochem. J., 155, 217 (1976).
12. S. Nakagawa, S. Kumin, and H. M. Nitowski, Biochim. Biophys. Acta, 101, 33 (1980).
13. D. J. Opheim and O. Touster, J. Biol. Chem., 253, 1017 (1978).
14. T. Tanaka, M. Kobayashi, and T. Usui, Hiroshima J. Med. Sci., 32, 207 (1983).

EFFECT OF MONONUCLEAR PHAGOCYTE SYSTEM DEFICIENCY AND OF YEAST POLYSACCHARIDE INJECTIONS ON HETEROTOPIC BONE MARROW FORMATION

S. V. Gurina, I. N. Ivasenko, M. A. Kashkina, A. Yu. Zaritskii, and G. E. Arkad'eva

UDC 616.419-089.843-092.9-07:616.419-003.971-007.415-031.84-02:616.155.33-008.13

KEY WORDS: mononuclear phagocyte system; heterotopic focus of hematopoiesis; polysaccharide.

Processes of hematopoiesis, controlled by secretion products of monocytes and macrophages [7, 9] and normally taking place in an ectopic focus, are disturbed as a result of blood loss or irradiation of the recipients [4]. The cause of this destabilization of hematopoiesis may also be deficiency of the mononuclear phagocyte system (MPS) which may arise for various reasons (as a result of disease, or created artificially). One model of artificially created MPS deficiency is based on chronic drainage of the peritoneal cavity of mice, with the use of an irrigating solution. Under these circumstances the quantitative and qualitative parameters of function of mononuclear phagocytes are disturbed [6].

This paper describes the results of a study of the effect of MPS deficiency on the formation of a heterotopic focus of hematopoiesis and of the action of yeast heteropolysaccharide, a stimulator of MPS, under these conditions [2].

EXPERIMENTAL METHOD

The extracellular heteropolysaccharide produced by *Cryptococcus luteolus*, strain 228 [1], was used. Experiments were carried out on 120 male (CBA × C57BL)F_1 mice; the peritoneal cavity of 50 mice was drained by the method described in [6] to exhaust MPS. Half of the mice subjected to irrigation in this way were used as donors of bone marrow (donors with MPS deficiency), which was implanted beneath the renal capsule of intact recipients. The other half of these animals were used as recipients of bone marrow from normal donors (the recipients had MPS deficiency). The polysaccharide was injected into these and other recipients intraperitoneally for 30 days after implantation of bone marrow, in a dose of 25 mg/kg every 7 days. Control recipients were given injections of physiological saline.

The heterotopic foci which formed were compared with foci in intact recipients, in which bone marrow from intact donors was implanted. The mice were killed by dislocation of the spine 30 days after implantation of bone marrow. The dimensions of the heterotopic foci formed were estimated from the number of cells and the weight of the bony capsule. The number of hematopoietic cells in the femoral medullary cavity also was determined.

EXPERIMENTAL RESULTS

After drainage for 10 days the number of cells in the peritoneal cavity was appreciably reduced (Table 1). After 30 days the content of peritoneal cells was increased by 1.3 times, although it was still only half the original value.

Academician I. P. Pavlov First Leningrad Medical Institute. Leningrad Pharmaceutical Chemical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR N. P. Bekhtereva.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 106, No. 7, pp. 95-97, July, 1988. Original article submitted January 23, 1987.

 0007/4888/88/0007-1026$12.50

TABLE 1. Changes in Number of Cells in Femoral Medulla and Peritoneal Cavity of Mice After Prolonged Drainage and Injection of Polysaccharide (M ± m)

Location	Number of cells × 10^6 after 30 days			
	initial	after drainage for 10 days	injection of 0.14M NaCl	injection of polysaccharide
Peritoneal cavity	1,50±0,18	0,60±0,06*	0,80±0,05	1,46±0,13
Femoral medulla	11,2±0,6	15,3±0,7*	15,4±0,6	12,4±0,7

Legend. Here and in Tables 2 and 3: *$p < 0.05$.

TABLE 2. Effect of Polysaccharides on Heterotopic Focus Formation in Intact Recipients into Which Bone Marrow from Donors with MPS Deficiency Had Been Implanted (M ± m)

Parameters of size of focus	Intact donors		Donors with MPS deficiency	
	injection of 0.14M NaCl (control)	injection of polysaccharide	injection of 0.14M NaCl (control)	injection of polysaccharide
Number of cells × 10^6	5,6±0,9	10,0±1,6*	5,2±1,0	8,6±1,2*
Weight of bony capsule, mg	1,2±0,1	2,0±0,3	0,9±0,2	0,9±0,2

TABLE 3. Changes in Dimensions of Heterotopic Focus of Hematopoiesis after Injection of Polysaccharide into Recipient Mice with MPS Deficiency (M ± m)

Parameters of size of focus	Intact recipients	Recipients with MPS deficiency	
	injection of 0.14 M NaCl (control)	injection of 0.1 M NaCl (control)	Injection of polysaccharide
Number of cells × 10^6	5,6±0,9	10,8±2,0*	6,1±0,9
Weight of bony capsule, mg	1,2±0,1	2,1±0,2*	1,5±0,2

The number of hematopoietic cells in the femoral medullary cavity was significantly increased as a result of irrigation ($p < 0.01$) and it remained at that level for 30 days, until the end of the experiments. This was evidence on the whole that the reproducibility of the method was adequate. Injection of the polysaccharides restored the above-mentioned parameters to their original level (Table 1).

When 30 days had elapsed after transplantation of bone marrow from mice subjected to prolonged irrigation of the peritoneal cavity, the dimensions of the heterotopic foci, measured according to the number of cells and the weight of the bony capsule, were unchanged compared with foci in control animals, into which bone marrow from intact donors was implanted (Table 2). Probably the MPS deficiency did not affect transplantable precursor cells of the hematopoietic stroma, leading to the formation of an ectopic focus in the recipient mice. Weekly injections (for 30 days) of polysaccharide into these animals led to an increase in the number of hematopoietic cells in the heterotopic focus. The same effect occurred after injection of polysaccharides into recipients into which bone marrow from intact donors has been implanted, but under these circumstances the weight of the bony capsule also was increased (Table 2).

It can be postulated that the action of the polysaccharide caused strengthening of the distant regulation of the process of formation of the heterotopic focus of hematopoiesis. Distant factors of this kind could be biologically active substances secreted by polysaccharide-activated recipient's cells, mononuclear phagocytes for example [5, 8].

After implantation of bone marrow from intact donors with MPS deficiency, more intensive formation of heterotopic foci of hematopoiesis took place (Table 3) than in intact recipients (according to the number of cells and the weight of the bony capsule). Evidently just as in the case of irradiation [3, 4], the increase in size and the heterotopic focus was due to the stimulating effect of the recipient's humoral factors on the more mature, untransplantable

precursor cells of the hematopoietic stroma. Under the influence of the polysaccharide, in mice with MPS deficiency there was a decrease in size of the heterotopic focus, to the level observed in intact animals (Table 3), which could be connected, under conditions of MPS deficiency, with the direct inhibitory effect of the polysaccharide on osteogenic and hematopoietic precursor cells.

Injection of the polysaccharide into recipient mice with MPS deficiency led to a decrease in the number of cells and in the weight of the bony capsule of the heterotopic focus down to the level observed in intact animals (Table 3), to a decrease in the number of hematopoietic cells in the femoral marrow, and to an increase in the number of cells in the peritoneal cavity up to its initial level (Table 1). Consequently, under these conditions the polysaccharide had an equalizing or regulatory action.

It can thus be concluded that in different states of an animal, the heteropolysaccharide studied in these experiments was characterized by an inhibitory or stimulating effect on the formation of a heterotopic focus of hematopoiesis. Moreover, the inhibitory effect of the polysaccharide under conditions of MPS deficiency restored the normal size of the enlarged heterotopic focus and the normal number of hematopoietic femoral marrow cells.

LITERATURE CITED

1. E. P. Anan'eva, G. A. Vitovskaya, N. P. Elinov, and N. A. Farbshtein, Chemistry and Biochemistry of Carbohydrates [in Russian], Pushchino (1980), p. 80.
2. G. E. Arkad'eva, I. S. Freidlin, M. A. Kashkina, et al., Results and Prospects of Scientific Research into Microbial Polysaccharides [in Russian], Leningrad (1984), p. 135.
3. O. A. Gurevich and I. L. Chertkov, Probl. Gematol., No. 2, 3 (1980).
4. O. A. Gurevich and I. L. Chertkov, Probl. Gematol., No. 8, 43 (1980).
5. G. K. Zakenfel'd, Results and Prospects of Scientific Research into Microbial Polysaccharides [in Russian], Leningrad (1984), p. 140.
6. V. D. Kravtsov, T. D. Zorina, G. E. Arkad'eva, and I. S. Freidlin, Immunologiya, No. 5, 48 (1985).
7. P. A. Chervenick and A. F. Lobuglio, Science, 178, 164 (1972).
8. M. L. Patchen and E. L. Lotzova, Exp. Hemat., 8, 409 (1980).
9. F. W. Rusceffi and R. L. Gallo, Blood, 87, 379 (1981).

EFFECT OF DALARGIN, A STABLE LEU-ENKEPHALIN ANALOG, ON CELL DIVISION IN THE ALBINO RAT CORNEAL EPITHELIUM

T. D. Pan'kova, S. S. Timoshin, M. I. Radivoz, and M. I. Titov

UDC 612.841.0143:612.6.014.43

KEY WORDS: enkephalins; dalargin; DNA synthesis; cell division.

Dalargin, a stable synthetic analog of Leu-enkephalin, is considered to be one of the most effective preparations against peptic ulcer [2, 5]. Besides its action on the endocrine system [3] and its immunomodulating properties [1], an important role in the therapeutic effect of dalargin is ascribed to its ability to act on proliferative processes. In previous investigations the writers showed that administration of dalargin stimulates DNA synthesis in epithelial tissues. In some cases, however, an appropriate increase in the mitotic index was not observed. It has been suggested that under these circumstances mitosis itself is accelerated or a circadian disturbance of coordination between DNA synthesis and entry of the cells into mitosis takes place. It was also difficult to rule out long delay of the cells in the G_2 period or polyploidization of the cells.

Central Research Laboratory, Khabarovsk Medical Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Val'dman.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 106, No. 7, pp. 97-99, July, 1988. Original article submitted June 9, 1987.

0007-4888/88/0007-1028$12.50