# EFFECT OF DRUGS ACTING CHIEFLY ON PERIPHERAL MUSCARINIC CHOLINERGIC SYSTEMS ON BONE MARROW EOSINOPHILS

Yu. B. Deshevoi and P. D. Gorizontov

UDC 612.112.92.014.46:615.217.32

KEY WORDS: atropine; aceclidine; muscarinic acetylcholine receptors; eosinophils; bone marrow.

There is some evidence in the literature that cholinergic systems can participate in maintenance of the blood eosinophil level *in vivo*. However, it is not at all clear from these findings at what level (bone marrow eosinophils, blood cells, migration of eosinophils from the circulation into the tissues) this possible regulation takes place.

Clinical investigations have confirmed a connection between an increase in the blood eosinophil count and elevation of the tone of the parasympathetic nervous system. Injection of atropine into guinea pigs also caused eosinopenia within 2-6 h of the first injection. Conversely, injection of the muscarinic cholinomimetic mecholine or of the anticholinesterase agent physostigmine caused a rapid increase in the blood eosinophil count [6, 9, 10]. Injection of physostigmine alone or of physostigmine together with acetylcholine into dogs in most cases reduced the blood eosinophil count [8]. Injections of another anticholinesterase drug, prostigmine, into guinea pigs also caused eosinopenia within a few hours [6].

This paper gives data on the effect of cholinotropic drugs acting chiefly in the region of peripheral muscarinic cholinergic systems on bone marrow eosinophils. No such investigations could be found in the literature.

## EXPERIMENTAL METHOD

Experiments were carried out on 450 female Wistar rats weighting 160-190 g. Atropine sulfate, in doses of 50, 100, and 150 mg/kg (dissolved in 1 ml sterile water for injections) was injected once only, and aceclidine in doses of 5, 10, and 15 mg/kg (dissolved in 0.5 ml water) was injected five times, at intervals of 3 h, because of its short period of action. Both drugs were injected subcutaneously. Their doses were pharmacologically active and nontoxic [1, 4]. Sterile water for injections was injected into the control animals in the same volume and in the same order as into the experimental rats. The rats were decapitated 3, 6, 9, 12, and 24 h after the injections. The total number of cells in the femoral marrow was studied. The percentage of eosinophils (in 1000 nucleated cells) was determined in bone marrow squash preparations and differential eosinophil counts also were undertaken (on 200 eosinophils). Next, knowing the total number of karyocytes in the femur and also the relative percentages of eosinophils, the absolute numbers of eosinophils of different degrees of maturity were calculated. Blood samples for determination of the peripheral blood eosinophil count were taken from the tail. The absolute number of eosinophils in the blood was counted in a Fuchs—Rosenthal chamber by the method in [5]. The numerical results were subjected to statistical analysis. Significance of differences was determined by means of confidence intervals calculated at the $P = 0.05$ level.

## EXPERIMENTAL RESULTS

Blocking peripheral muscarinic acetylcholine receptors by atropine led to a sharp increase (200-230% of the initial level) in the number of eosinophils in the bone marrow. By contrast to this effect stimulation of peripheral muscarinic acetylcholine receptors with aceclidine caused a marked decrease (almost by half) in the number of eosinophils in the bone marrow. Changes were observed as early as 3-6 h after the beginning of injection of the drugs. Fluctuations in the eosinophil content in the bone marrow were mainly attributable to

Institute of Biophysics, Ministry of Health of the USSR, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 94, No. 11, pp. 61-63, November, 1982. Original article submitted March 16, 1982.

0007-4888/82/9411-1539$07.50  

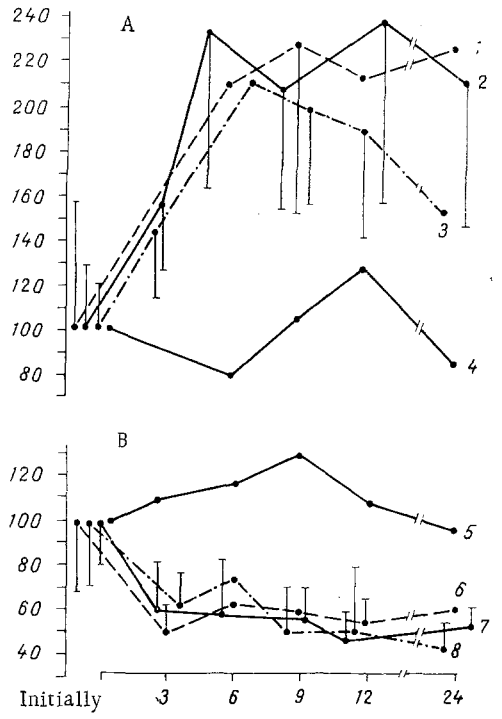


Fig. 1

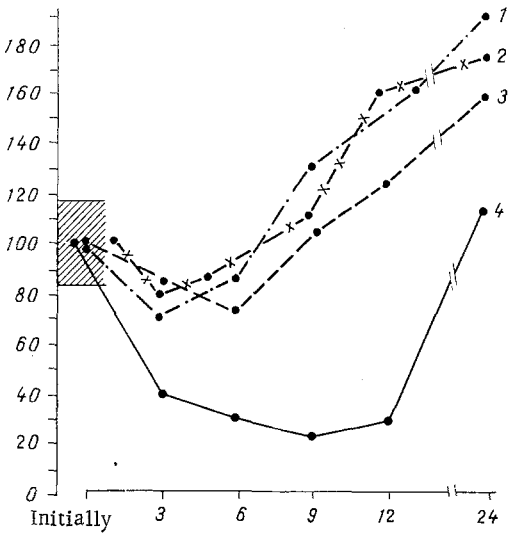


Fig. 2

Fig. 1. Number of mature eosinophils in femoral marrow after injection of atropine (A) and aceclidine (B). Abscissa, time after beginning of injections (in h); ordinate, number of cells (in % of initial level). 1, 2, 3) Atropine in doses of 100, 150, and 50 mg/kg respectively; 4, 5) control, 6, 7, 8) aceclidine in doses of 15, 5, and 10 mg/kg respectively. Vertical lines denote confidence intervals.

Fig. 2. Peripheral blood eosinophil count after injection of aceclidine in a dose of 10 mg/kg five times at intervals of 3 h (1), of water for injections in a dose of 0.5 ml, five times (2), and in a dose of 1 ml, once (3), and of atropine in a dose of 100 mg/kg, once (4). Shaded area indicates confidence interval for intact animals. Each point indicates mean data for 9-11 rats. Legend for ordinate and abscissa as in Fig. 1.

the number of mature stab and segmented eosinophils (Fig. 1). The rapid rise or fall in the number of mature eosinophils in the bone marrow after injection of the drugs is more likely to indicate the influence of peripheral muscarinic cholinergic systems on the migration of mature eosinophils from the bone marrow into the circulating blood. This suggestion is confirmed by direct numerical studies of peripheral blood eosinophils. The results of this investigation showed, first, a sharp decline in the number of eosinophils in the blood after injection of atropine, evidently as a result of delay of migration of mature eosinophils from the bone marrow, and also, possibly their rapid removal from the circulation, and second, an increase in the number of eosinophils after injections of aceclidine, probably due to their mobilization from the bone marrow (Fig. 2).

Injection of sterile water (water for injections) also caused eosinophilia in the blood at the same times and to the same degree as aceclidine (Fig. 2). The increase in the number of eosinophils in the blood after injections of water was evidently due to their redistribution within the blood stream, for the number of mature eosinophils in the bone marrow was virtually the same as after injection of aceclidine (Fig. 1).

The results thus show that peripheral muscarinic cholinergic systems of the body are involved in regulating the migration of mature eosinophils from the bone marrow into the circulating blood. However, the mechanisms of this effect are not clear and require further study.

## LITERATURE CITED


1. V. V. Gatsura and A. S. Saratikov, Pharmacological Agents in Experimental Medicine and Biology [in Russian], Tomsk (1977).
2. I. A. Kassirskii and G. A. Alekseev, Clinical Hematology [in Russian], Moscow (1970), p. 775.
3. P. S. Moderatov and M. V. Kukharenko, Kazan. Med. Zh., No. 1, 59 (1934).
4. G. N. Pershin (ed.), New Therapeutic Substances [in Russian], No. 2, Moscow (1962), p. 14.
5. I. S. Piralishvili, Lab. Delo, No. 3, 20 (1962).
6. C. D. Caplovitz, Texas Rep. Biol. Med., 5, 383 (1947).
7. W. Falta and F. Kahn, Z. Klin. Med., 74, 108 (1912).
8. C. T. Harwood and J. W. Mason, Am. J. Physiol., 186, 445 (1956).
9. L. Lengyel, Acta Neuroveg. (Vienna), 27, 212 (1965).
10. L. Lengyel, Acta Neuroveg. (Vienna), 27, 219 (1965).