

It may be concluded from the electrocardiographic findings, from the morphological study of the thermal lesions, which are seen to be sharply demarcated, and to be remote from the locations of the intracardial nervous apparatus, and from the rapid development of the changes in this apparatus, that these alterations are not ascribable to the direct action of the traumatizing agent, but that they arise reflexively, as a result of the powerful additional stimuli proceeding from the focal lesion.

The stimuli from the focal lesion may reach the intracardial nervous apparatus through existing reflex arcs, involving the second, intact vagus nerve, the intervertebral ganglions, and the sympathetic nerve. Of equal importance may be links of the axon reflex type, and this view is supported by A. A. Zubkov's comparative morphological studies [2]. Phenomena of the type of perielectrotonic remote action may also be of some significance [7].

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#### ALTERATIONS IN PHAGOCYTIC ACTIVITY OF THE LEUCOCYTES OF HUMAN BLOOD DURING ANESTHESIA

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Numerous papers have been published over the past few years on the effect of the nervous system on immunobiological processes, and, in particular, on the phagocytic reaction of leucocytes [5, 10, 11, 12, 13]. Most of the researches were performed on animals, and only a few [4, 9, 11] are based on observations of human subjects.

The present paper presents the results of observations of phagocytic activity of the leucocytes of 127 patients under ether or nitrous oxide anesthesia. The complement activity of the blood was also studied for some of the patients.

#### EXPERIMENTAL METHODS

Phagocytic activity and complement titer were determined in 110 patients before administration of the narcotic, during the stage of unconsciousness preceding the operation, and on the day following the operation. Of these patients, 81 underwent surgical operations for conditions such as contractures, ankyloses and skin defects, i.e., they were not suffering from inflammatory or septic conditions. The complement titer of the blood was determined by the same method as is used in the Wasserman reaction. The phagocytic activity of the leucocytes was assessed with respect to *Staphylococcus aureus*, strain 209. To a mixture of 0.02 ml of 3.8% sodium

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\* In Russian.

citrate solution and 0.08 ml of blood we added 0.05 ml of a staphylococcus suspension (containing  $2 \times 10^9$  organisms per ml) in physiological saline, and the mixture was incubated at 37° for 20 minutes. A smear was then made (fixed with Nikiforov's mixture, stained with methylene blue), and counts were made on 5 smears, each of 20 leucocytes. A shift in the phagocytic number (number of cocci taken up per leucocyte) was taken as significant if it exceeded the initial (preanesthesia) value by more than 10%.

## EXPERIMENTAL RESULTS

Observations on 25 patients showed that the complementary activity of the blood did not vary beyond the limits of accuracy of the determination, irrespective of the nature or the amount of the anesthetic used, and we did not proceed further with this aspect of the investigation.

Of 94 patients examined on the day following the operation, 57 had a phagocytic number lower than before administration of the anesthetic, 14 showed the same value, and 21 a higher one. Since these data represent not only the effects of anesthetization, but also of the surgical treatment, we shall not here discuss them.

An examination of the material showed that the variations in phagocytosis were not correlated with the nature of the anesthetic, or with the amount of it used, or with the existence of any septic process in the patient. Thus the phagocytic index for patients receiving nitrous oxide rose in 14, fell in 89, and was unchanged in 4 cases. The corresponding figures with ether anesthesia were 8, 42, and 3.

Rise in phagocytic index was observed in 19 patients not presenting septic complications, a fall in 57, and no change in 5 patients. The corresponding figures for patients with sepsis were 3, 42, and 2.

Blood was taken for the second examination when the patient was under anesthetic, shortly before the operation. In 21 patients, however, the blood samples were taken at the end of the stage of excitation, as the operations were begun before the patient was deeply unconscious; in 17 of these phagocytosis was higher than the initial value, in 2 lower, and unchanged for the remaining two. The other 89 patients were fully anesthetized at the time of blood sampling: increased phagocytosis was seen in only 5 patients of this group, and no change in 5, while the index was markedly lowered for the remaining 79 patients.

In connection with these findings, we made a special examination of a further 17 patients, with the object of elucidating the effect of the stage of excitation on the phagocytic activity of leucocytes, and of determining whether the lowered phagocytosis observed during anesthesia is not only a relative effect; the emotional state of the patient of the day of the operation, and while waiting for it, may have exerted a stimulatory effect of phagocytic activity, and the apparent fall during the action of the anesthetic may have been only a reversion to the normal level.

The phagocytic activity of these patients was twice determined during the week preceding the operation, a third time immediately before the operation, and twice while the patient was under the anesthetic, once at the height of the stage of excitation, and once during profound sleep. In 3 patients only was the phagocytic activity different (higher) from that found during the previous week. This is evidence of the incorrectness of the supposition that the phagocytic activity of these patients was at an abnormally high level when they entered the operating theater and the subsequent fall might have been no more than a return to the normal value.

The phagocytic index during the stage of excitation was raised in 10 of 17 patients, unchanged in 4, and lowered in 3 cases. During profound anesthetic sleep 15 of the 17 patients showed a definite lowering of the index, as compared with both the preanesthetic state and with that of excitation. In one case only was it raised, and in one case unchanged.

Apart from our observations on patients, we performed control experiments, with the object of ascertaining whether ether, at the dosage levels used, has any direct effect on leucocytes, leading to change in their phagocytic activity. Blood was placed in a hermetically sealed glass vessel, under an atmosphere containing a concentration of ether vapor (2.8 mg per ml) which would cause profound narcosis in the human. After 30 minutes of contact with the vapor we could not find any change in the phagocytic activity of the leucocytes.

It thus appears that ether or nitrous oxide anesthesia leads to a rise in the phagocytic activity of leucocytes during the stage of excitation, and to a fall during that of profound unconsciousness. The question arises as to how these central nervous system effects can be transmitted to the leucocytes, which have no direct connection with the nervous system.

The work of N. V. Puchkov, G. V. Golodets, and others [3, 6, 8] has shown that mediators can exert a significant action on the phagocytic activity of leucocytes: sympathicotropic substances stimulate phagocytosis, while vagotropic ones (acetylcholine) depress it. M. Ya. Mikhelson's experiments [7] showed that narcotic substances exert a powerful inhibitory action on cholinesterase, both in vivo and in vitro. It might be supposed that anesthetics cause a rise in the acetylcholine content of the tissues, and hence to an inhibition of phagocytosis. When the blood samples were taken during the stage of excitation, in which the tonus of the sympathetic system was raised, the increased production of sympathicotropic substances heightened the phagocytic activity of the leucocytes.

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#### EFFECT OF BARBITURATES ON THE DIFFERENTIAL CELL COUNT OF PERIPHERAL BLOOD OF NORMAL ANIMALS AND IN EXPERIMENTAL ANEMIA

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The present paper gives the results of an investigation into the effects of some barbiturate hypnotics on the differential cell count of peripheral blood. It is a continuation of earlier published researches [1].

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