EFFECT OF VACCINATION AGAINST TUBERCULOSIS ON BLOOD TRANSFUSION SHOCK

(UDC 616-001.36-02:615.38]-02:616-002.5-084.47)

G. S. Kan and E. L. Kan

Laboratory of Experimental Pathology and Therapy (Head, G. S. Kan), Leningrad Research Institute of Tuberculosis (Director, Professor A. D. Semenov)
(Presented by Academician V. N. Chernigovskii)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 57, No. 6, pp. 64-69, June, 1964
Original article submitted February 4, 1963

The investigation of the physiological mechanisms of immunity to tuberculosis has made it imperative to elucidate the effect of vaccination with a BCG strain on the resistance of the various systems of regulation to the harmful action of specific antigenic stimuli. As a result of the transfusion of heterogenic blood profound changes develop in the vital activity of the organism as a result of stimulation of the chemoreceptor apparatus by changes in the colloid state of the proteins, the reaction to incompatible proteins, and so on [1,8]. Blood transfusion shock develops, in consequence of the successive involvement of the various divisions of the nervous system by the action of the above-mentioned factors, mainly by means of a reflex mechanism [3, 5-9], and also as a result of the direct action of the heterogenic blood and of secondary toxic substances on other links of the nervous system, including efferent mechanisms maintaining vascular tone [2,4].

In the present study the course of blood transfusion shock was investigated in animals vaccinated against tuberculosis. The principal test was registration of the blood pressure, the mechanisms of regulation of which to some degree characterize the general resistance of the organism to a pathogenic stimulus. The resistance of the mechanisms of regulation of respiration and the survival rate of the animals were also studied.

METHOD

Observations were made on 98 rabbits, of which 20 were controls and 78 were vaccinated with a BCG strain intradermally in a dose of 10 mg of dried vaccine per animal. On the 7th, 14th, 21st, 31st, 43rd, 53rd, 75th, 91st, and 102nd days after vaccination, in an acute experiment without anesthesia, the experimental animals received an injection of stored donors' blood of group 0 (I) in a volume of 10.7-11.0 ml/kg body weight into the jugular vein. Control experiments on healthy rabbits were conducted in a similar manner. Recordings of the blood pressure (in the common carotid artery), respiration (in the trachea), and the period of survival in cases in which the experiment terminated in death were made on the drum of a kymograph.

RESULTS

Immediately after the transfusion of heterogenic blood the control animals developed uniform and considerable disturbances of the circulation and respiration. These disturbances were manifested in the first place by a sharp fall in the level of the arterial pressure after a relatively short latent period with a mean duration of 7 sec. As a rule the level of the arterial pressure in this (the 1st) phase of the reaction rose on the average by 7 mm.

The duration of the 2nd phase of the reaction—the phase of a fall of the arterial pressure—amounted on the average to 1 min 55 sec. In all the experiments the arterial pressure fell to zero, causing death of the control rabbits. In the period of a fall in the arterial pressure the heart rate became slowed and the so-called vagus pulse sometimes supervened. As a rule, against this background of a fall of arterial pressure, slight or sometimes very marked periodic changes in its level took place.

The disturbances of respiration taking place in response to the transfusion of heterogenic blood were manifested in all the experiments by inhibition of the respiratory movements at the end of the experiment. Respiratory arrest

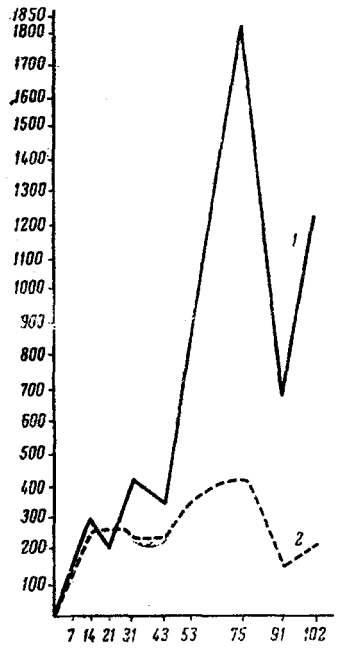

Fig. 1. Duration (1) and magnitude (2) of 1st phase of changes in level of arterial pressure arising in response to transfusion of heterogenic blood at different intervals after vaccination. Along the axis of ordinates—deviation of indices (as a percentage of control value); along the axis of abscissas—time after vaccination (in days).

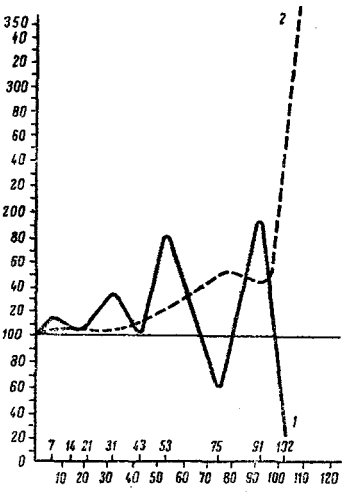

Fig. 2. Duration and reciprocal of maximal fall in level of arterial pressure in 2nd phase of reaction to transfusion of heterogenic blood at various intervals after vaccination. 1) duration of 2nd phase of reaction of arterial pressure; 2) reciprocal of maximal fall in level of arterial pressure, calculated as a percentage of control (also expressed as a percentage).

during total inhibition developed at the neutral point between the maximal inspiration and expiration. In some cases a few respiratory movements of considerable magnitude were observed against the background of respiratory arrest. This final phase of the reaction of the respiration, occupying a large part of the period of the reaction of the organism to the transfused blood, was preceded by a relatively short, or sometimes rather protracted phase of excitation of respiration. It was manifested, as a rule, by an increase, sometimes extremely rapid, in the amplitude of the respiratory movements, and more rarely by a simultaneous increase or decrease in the frequency of the respiratory movements.

Different results were obtained in experiments on preliminarily vaccinated rabbits. The injection of heterogenic blood in these experiments also led to changes in the circulation and respiration in most experiments, terminating in death. Meanwhile these changes were less severe than in the controls and were dependent on the time elapsing after vaccination. These changes will first be considered from the example of the reaction of the arterial pressure, for it is here that they find their most accurate quantitative expression.

The latent period of the 1st phase of the changes in the level of the arterial pressure caused in the heterogenic blood was identical at all periods of observation after vaccination with that in the control animals, and remained within the limits of 0-2 sec. On ther other hand, substantial changes took place in the duration of the initial, pressor phase of the reaction of the arterial pressure. By the 7th day after vaccination it had risen by almost 50% over the control level, after 2 weeks by 200%, and it continued to rise in a fluctuating manner thereafter. The maximum increase, observed on the 75th day after vaccination, was 1821%. In still later periods, on the 102nd day after vaccination, this increase was slightly less marked, but it remained very impressive, amounting to 1214% of the control value (Fig. 1).

The amplitude of this phase also showed changes. The rise in the level of the arterial pressure exceeded that in the controls. On the 7th day after vaccination, for instance, this difference was only 8.5%, but on the 14th day the rise in pressure in the experimental animals was 257% of the control level. Subsequently, until the 102nd day,

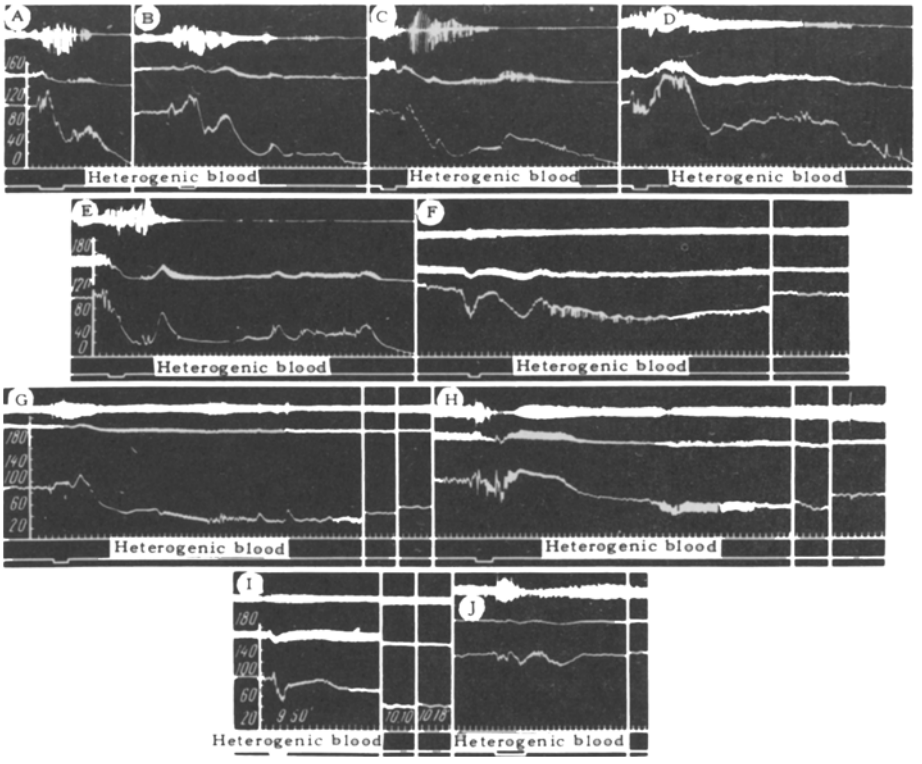

Fig. 3. Changes in level of arterial pressure and in respiration in rabbits arising in response to transfusion of heterogenic blood at various intervals after vaccianation. A) control experiment; B) 7th day after vaccination; C) 14th day; D) 21st day; E) 30th day; F) 45th day; G) 53rd day; H) 75th day; I) 91st day; J) 106th day. Significance of curves on kymograms (from top to bottom): respiration; arterial pressure in carotid artery (tonometer); arterial pressure in carotid artery (mercury manometer); time marker (5 sec); marker of stimulation.

the magnitude of the pressor reaction, while fluctuating, continued to exceed that in the control series by 50-150% or, in some cases, by 300% (on the 75th day after vaccination) (see Fig. 1).

Important changes also took place in the 2nd, depressor, phase of blood transfusion shock. The latent period of this reaction increased, which was due to a change in the duration of the 1st (pressor) phase of the reaction of the arterial pressure in the preliminarily vaccinated animals. Changes also occurred in the duration of the depressor phase (in the case of the subsequent restoration of the level of the arterial pressure it was measured from the moment of onset of the fall in pressure to the time at which the lowest level was reached in the course of the reaction). Almost throughout the period of observation after vaccination the duration of the period of increasing depression exceeded that in the control series. Not until the 75th and 102nd days after vaccination did the maximum of the fall in arterial pressure in the experimental series develop more rapidly than in the control series (by 39 and 69%) (Fig. 2).

Consistent changes also took place in the principal index of the stability of the system stabilizing the level of the arterial pressure, in the vaccinated animals—the reciprocal of the maximal fall in the level of the arterial pressure, expressed as a percentage of the control value (this index was also calculated as a percentage).

By the 7th day this index showed a small increase in value amounting to 4%. Subsequently, until the 31st day, the increase varied within the range of 3-5%. Later an appreciable, although initially gradual, increase in the stability of the level of the arterial pressure to the shock-producing action of the heterogenic blood began to take place. This was shown by the fact that the increase in this index on the 43rd day was 15%, on the 53rd day 26%, and during the 3rd month it remained between 48 and 54%, while on the 102nd day it reached extremely high values, exceeding the control value of this index by nearly 250% (see Figs. 2 and 3).

In the experiments which did not terminate in death of the vaccinated rabbits from shock, immediately after the maximal decrease in the level of the arterial pressure it began to rise again gradually. In 9 cases full recovery

of the arterial pressure was observed to its initial level. This occurred in 7 experiments in the course of 10-25 min, and in 2 experiments in the course of 2-3 min. In the remaining rabbits a partial recovery of the level of the arterial pressure was observed, reaching 40-80% of its initial level after 8-12-20-25 min (see Fig. 3).

In the vaccinated rabbits, not only the vasomotor, but also the respiratory component of blood transfusion shock differed from that in the controls. In cases terminating in death of the experimental rabbits the reaction of respiration was indistinguishable from that in the controls from the qualitative point of view. The only feature of note (not in all the experiments) was a lengthening of the initial phase of the changes in respiration and a shortening of the phase of its inhibition by comparison with the control values.

In the rabbits which did not die from shock, in some cases the 1st phase of the disturbances of respiration was indistinguishable from that in the controls. In some experiments it was modified: immediately after the transfusion of heterogenic blood transient reversible signs of excitation of respiration or reversible signs of inhibition of respiration appeared. In the 2nd phase, as a rule, the amplitude of the respiratory movements in the surviving animals increased and the rate of respiration sometimes rose. Restoration of the original respiration in this group of animals in some cases preceded the restoration of the original level of the arterial pressure.

The growth of resistance of the rabbits vaccinated with BCG to transfusion of heterogenic blood was also expressed as a change in the survival rate. In the controls, for instance, not one of the 20 animals survived after transfusion of heterogenic blood. Meanwhile, of the 78 vaccinated rabbits, 30 died from shock at various intervals after vaccination. In the 1st month after vaccination the growth of the resistance of the animals to blood transfusion shock was still only very ill defined (only 4 of the 27 rabbits survived). By the 45th-53rd day it had risen considerably (10 of the 30 rabbits survived). The resistance of the animals to shock rose significantly to the 75th-91st day after vaccination (9 of the 14 rabbits survived). Finally, in the experiments conducted on the 102nd day after vaccination, not one of the rabbits died from shock. Consequently, the behavior of this index also shows that the resistance to blood transfusion shock increases gradually after vaccination and reached its maximal degree after the middle of the 2nd month. At the beginning of the 4th month after vaccination the resistance again increases considerably.

Hence, vaccination with a BCG strain leads to a gradually increasing resistance of the organism to blood transfusion shock. The increase in the resistance to the harmful action of the nonspecific antigenic stimulus was especially marked in respect of the system stabilizing the level of the arterial pressure. This was manifested by an increase in the duration and magnitude of the phase of the initial increase in the arterial pressure, by a prolongation of the 2nd phase, and by a less marked fall in the level of the arterial pressure in this phase. The resistance of the system stabilizing the external respiration was also clearly increased.

The increase in resistance to blood transfusion shock was most clearly revealed in the period of fully formed specific postvaccinal immunity against tuberculosis (from the 43rd day after vaccination). It reached it maximum at the end of the 3rd or beginning of the 4th month after vaccination with BCG strain.

Data in the literature give grounds for supposing that the phenomena described above are mainly determined by the fact that vaccination against tuberculosis modifies the functional state of the nervous mechanisms maintaining homeostasis.

LITERATURE CITED

1. A. A. Bogomolets. In book: Current Problems in Hematology and Blood Transfusion [in Russian], No. 13-14, Moscow–Leningrad, (1936), p. 19.
2. P. N. Veselkin and M. I. Kuznetsovskaya. Sov. khir. 7, 2-3, (1934), p. 442.
3. V. S. Galkin. Narcosis [in Russian]. Kirov, (1944).
4. R. M. Glants. Nervous and Endocrine Factors of Regulation in the Mechanism of Action of Various Types of Hemotherapy. Author's abstract of doctorate dissertation, Khar'kov, (1960).
5. A. N. Gordienko. Role of the Carotid Sinus in the Development of Shock States [in Russian]. Krasnodar, (1948).
6. G. M. Gurevich and D. A. Kogan, Khirurgiya, 7 (1939), p. 3.
7. S. M. Pavlenko and A. L. Komendantova. Vrach. delo, 4, (1947), p. 251.
8. I. I. Fedorov. The Pathophysiological Bases of Blood Transfusion [in Russian]. Kiev, (1951).
9. V. N. Shamov and G. G. Karavanov. In book: A Handbook of Blood Transfusion (by V. N. Shamov and A. N. Filatov) [in Russian], Moscow–Leningrad, (1940), p. 532.