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THE EFFECT OF BIOGENESIS OF INTESTINAL MICROFLORA
ON THE DEVELOPMENT OF RADIATION SICKNESS
by G. G. Vasilenko and Y. Y. Nogachevskyy

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THE EFFECT OF BIOGENESIS OF INTESTINAL MICROFLORA
ON THE DEVELOPMENT OF RADIATION SICKNESS

[Following is a translation of an article by G. G. Vasilenko and Y. Y. Nogachevskyy in Mikrobiologichnyy Zhurnal (Microbiological Journal), Vol. 24, No. 5, Kiev, 1962, pages 35-38.]

A reduction in the natural and acquired immunity as a consequence of the effects of penetrating radiation on the microorganism creates the necessary conditions for changes in the normal biocenosis of the microflora of the organism. This manifests itself predominantly in the development of autoinfection (1-5). On the other hand, the influence of the state of biocenosis of the normal, especially the intestinal, microflora of the irradiated organism on the development of radiation sickness has been studied very little. Of primary interest here is the question of the presence of latent infections, the interconnections which develop between this state and the microbes which are the constant inhabitants of the intestine, against the background of changes caused by irradiation. A reduction in the natural resistance of the organism enables the microbes of the intestine to become aggressive and, breaking through the weakened natural barriers, to give rise to the development of autoinfection. Of particular importance with respect to the microbes of various species in the development of autoinfection is the original state of the biocenosis of the microbes of the intestine during irradiation.

In the present report, we shall take up the question of autoinfection in irradiated animals without a latent carrier state and also in the presence of such a state. The uniqueness of the biocenosis of the microbes of the intestine is due to the presence in the intestine of bacteria of the salmonella group.

Studies were performed on 220 irradiated and 120 nonirradiated mice. Radiation sickness was induced by total single irradiation of the animals under the following conditions: kv-190; ma-10; filter-0.5 mm copper and 1 mm aluminum; skin-focal distance-30 cm; time-9.3 minutes; total dose-500 r.

In these studies we used animals with latent infection and also without it, which were irradiated and maintained under identical conditions. As one of the signs of radiation sickness which enabled us to judge its development and course, we observed leukopenia.

The number of leukocytes was investigated in all mice before irradiation, as well as every three to five days after irradiation. Each time we computed the arithmetic mean, with the value prior to irradiation being taken as 100% (14,200). With respect to this we calculated the percentage of leukocytes in the blood of the irradiated animals. We also make observations of the general condition of both the experimental and control animals. Moreover, every five days following irradiation, up to the fiftieth day, we sacrificed mice in groups, which enabled us to perform observations on the different stages of the development of radiation sickness. Bacteriologic studies were carried out both on the sacrificed animals as well as on those which died spontaneously. Samples of all organs, blood, and intestinal contents were cultured on meat-peptone agar, Endo's medium, and Ploski'ova's medium. In this way we were able to assess the degree of dissemination of microbes among the various organs and blood, as well as to compare the relative contributions of the microflora thus recovered with the microflora of the small and large segments of the intestine. The microbes which were cultured bacteriologically were studied biochemically and serologically.

The first series of studies was performed on 168 irradiated mice with a natural latent salmonella carrier state, which was due to the Gertner bacillus. With respect to the degree of autoinfection, all animals were subdivided into three groups.

In cases in which microbes were recovered from all organs and from the blood, autoinfection was considered to be complete. As a rule, this led to death of the mice. Complete autoinfection was demonstrated in 50% of the mice with a latent carrier state. If microbes were isolated from the lymph nodes and the spleen, or less frequently, from the liver and not from the blood, then autoinfection was considered to be partial. This gave rise to a milder course of the infectious process. In this case, two eventualities were possible: one, a transition to complete autoinfection or self-purification of the organism from the infection. Partial autoinfection was demonstrated in 25.6% of the mice. The third group was found to be noninfected (24.4%). In this group, the mice did not die (see table).

Of importance is the fact that, in the presence of complete autoinfection, the relative composition of the microbes isolated from the organs and the blood was, as a rule, comparable to the composition of the microbes which were recovered from the contents of the initial segments of the small intestine. In all animals, cultures of the contents of the small intestine yielded massive growth.

Forms of Infection in Mice with Latent Infection

Forms of Infection	Died		Sacrificed		Total	
	Absolute Number	%	Absolute Number	%	Absolute Number	%
Complete autoinfection	71	92.2	13	14.3	84	50.0
Partial autoinfection	6	7.8	37	40.7	43	25.6
Absence of infection	--	--	41	45.0	41	24.4
Total	77	100	91	100	168	100

In cases of partial autoinfection, as well as in its absence, cultures from the small intestine ordinarily yielded negligible growth of colonies.

Hence, depending on the degree of contamination of the upper segments of the small intestine, the form of autoinfection was different. Apparently, radiation injury is accompanied by a spread of microbes from the lower segments of the large intestine into its upper segments and into the small intestine, which is one of the conditions of the development of autoinfection. Hence, one of the consequences of irradiation is a change in the microbial flora of the different segments of the intestine, which should be regarded as the principal change in the biocenosis of the intestinal microflora.

Moreover, the species composition of the microflora of the intestine and the mutual influences which are exerted by the species of microbes upon each other in the intestine also influences to a great extent the development of autoinfection following irradiation of the animals. Analysis of the bacteriologic studies for establishment of a connection between the character of the course of radiation sickness and the species of microbes which give rise to autoinfection, showed that, in the presence of complete autoinfection, the Gertner bacillus was isolated in 80.9% of cases, the enteric bacillus in 9.5%, and other microbes in 9.6% (Figure 1).

A different picture was observed in the case of partial autoinfection: in this, the enteric bacillus was most frequently isolated (51.2%); second place was occupied by the staphylococcus (32.5%); salmonella appeared in only 4.6% of the cases. Hence, we were able to establish a unique species composition of the microbes and of their distribution depending on the form of infection.

In order to study the normal biocenosis of the intestinal microflora in mice of a given group, we cultured the species of 60 living nonirradiated animals on appropriate media. Then we removed the colorless colonies. Four hundred fifty of these, with the aid of the

agglutination reaction, were shown to be colonies of salmonella enteritidis (agglutination with monoreceptor serum O-IX; H-gm). It turned out that 40% of the mice of this group were carriers of the salmonella enteritidis. Hence, the biocenosis of the intestinal microbes of these animals was composed of salmonella microbes and permanent representatives of the normal microflora. From this it follows that up to 40% of the mice in this group shown to have a latent salmonella infection. This circumstance enables us to demonstrate the importance of the microbial biocenosis in the development of autoinfection.

Under the same conditions and at the same times following the day of irradiation, the invasiveness of microbes of the intestine was found to be different. In the first place, the "open portal of infection" was penetrated by microbes of the latent infection--salmonella; the second place was occupied by enteric bacilli, and the third by cocci. It is possible that the presence in the intestine of salmonella inhibited the exhibition of aggressiveness in the other microbes, and since a salmonella carrier state was not found in all of the mice, then perhaps in cases in which it did not exist, other microbes were able to become aggressive. Hence, of importance in the intestinal biocenosis are the potential possibilities of each microbe to increase its own aggressiveness. In our studies, this was most obvious in case of salmonella enteritidis.

The second series of studies was performed on 52 mice of a healthy group. In cultures of the feces of these animals, the Gertner bacillus was not isolated; hence, there was no latent infection. Every five days, 7-8 mice were sacrificed and cultures were taken of the organs and of the blood. Complete autoinfection was not found in animals of this series. The mice did not die spontaneously. Partial autoinfection was demonstrated in 25% of the mice. The rest of them were not infected. In the case of partial autoinfection, enteric bacilli and staphylococcus were isolated in about equal numbers. A detectable leukopenia was demonstrated in the animals of this group only up to the tenth day following irradiation. This gives us reason to believe that leukopenia is associated with autoinfection, which in turn depends on the state of biocenosis of the intestinal microflora.

In comparing the degree of leukopenia and its duration in cases of latent infection and those without latent infection, it was found that, in the first instance, leukopenia lasts longer (up to the 35th day) whereas without latent infection the blood becomes normal by the 20th day following irradiation (Figure 2). The interconnection of these factors is illustrated by the results of this study: the absence of high aggressiveness of the intestinal microbes and the prolonged leukopenia gave rise to the benign course of radiation sickness in these cases.

Mice of the control group (60) were given intraperitoneal injections of cultures of Gertner bacillus. All of these died in the presence of sepsis. At the same time, there was a profound leukopenia in these animals. But compared with the irradiated mice with latent infection, the degree of this was less. This is a confirmation of the interconnection of these phenomena which, against a background of irradiation, becomes manifest to a greater degree.

Conclusions

- (1) Latent infection aggravates the course of radiation sickness: provocation of it is one of the major causes of generalized autoinfection and death of irradiated mice.
- (2) Under identical conditions, in animals without latent infection the aggressiveness of the intestinal microbes and the leukopenia are less pronounced.
- (3) Autoinfection in cases of radiation sickness, and the duration and degree of leukopenia depend, to a considerable extent, on the state of the biocenosis of the normal intestinal microflora.

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FIGURE APPENDIX

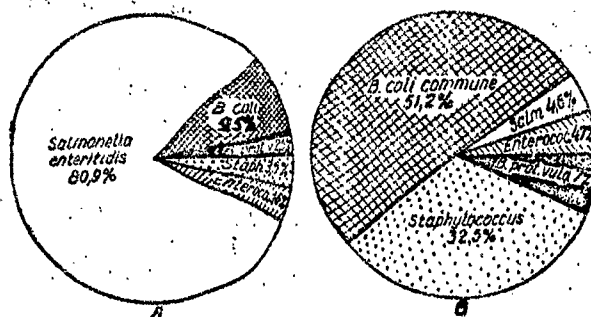


Figure 1. The Role of Different Species of Microbes in the Development of Autoinfection of Irradiated Mice in the Presence of Latent Infection. A - Complete autoinfection, B - Partial autoinfection.

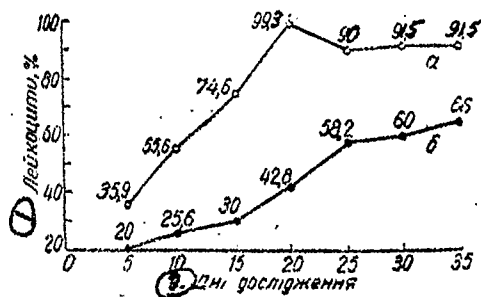


Figure 2. Leukopenia in Irradiated Mice without Latent Infection (a) and With Latent Infection (b). Legend: 1 - Leukocytes in percent, 2 - Days of Investigation.

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