ANESTHETIZATION IN RADIATION SICKNESS

TRANSLATED AND CONDENSED FROM THE REVIEW
BY PROFESSOR B. M. KHROMOV (LENINGRAD)
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THE EXTENSIVE utilization of roentgeno-radiotherapy as well as the utilization of atomic energy for peaceful and military purposes in recent years have intensified the interest of various medical specialists in the problem of radiation sickness. Undoubtedly, one of the most important problems is surgical anesthesia under conditions of the combined involvements. ["Combined involvements" is a term frequently used in the Russian literature; it indicates the combination of radiation and some other type of trauma.—*Editor.*]

The following associations of combined involvements should be distinguished: (1) thermal and mechanical trauma, (2) thermal trauma and radiation sickness, (3) mechanical trauma and radiation sickness, (4) thermal, mechanical trauma and radiation sickness. In addition, the possibility of infection or contamination of the wound surface by radioactive agents should be kept in mind. Such a combination is most expediently set apart into a special group of "radioactive mixtures." It is well known that, after the explosion of an atomic bomb, up to 200 radioactive isotopes are formed. These can infect wound surfaces at the time of the explosion proper, at the time of infliction of the trauma, or during the subsequent process of "settling" of radioactive particles of earth, dust and water. At this time surgery, whether necessitated by combined involvements or other reasons, must be performed in areas contaminated by radioactive agents. All of the conditions described above specifically influence the type of anesthesia and anesthetic technique to be used.

In discussing the indications for various types of anesthesia, we should consider the pathophysiological, pathological and clinical picture of combined involvement as well as the individual characteristics of the patient and the general-medical indications and contraindications. To be sure, the effects of various soporific and narcotic * agents on the course and outcome of radiation sickness should also be taken into account.

This translation and condensation of a review originally published in Russian is brought to the attention of our subscribers in order to provide them an insight into Russian medicine and to give them the benefit of information regarding a topic of vital importance. To conserve space, the 51 references to this review have not been reprinted but are available upon request from the office of *Anesthesiology.—Editor.*

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* In Russian, the word "narcotic" has a meaning nearer to the Greek from which the word comes; namely, "sleep-producing," and hence, is a more general usage than ours.—*Editor.*

Stages of Radiation Sickness

Understandably, the acute form of radiation sickness, which arbitrarily is divided into four stages, (periods) is of the greatest interest.

The First or Initial Stage (period of primary reactions) lasts from several hours to one to three to five days, depending on the dosage of irradiation. In the Japanese who were affected by the atomic explosion, it usually lasted one day, but in a number of cases dragged on to two days and more. During this period, a condition like drunkenness or general malaise, nausea, vomiting, dizziness and headache were seen. These signs subside gradually and the second stage begins.

The Second or Latent Stage (period of relative well-being) can last from several days to two to three weeks, depending on the severity of the involvement. Despite the apparent well being during this period, substantial functional changes occur in the body of the persons afflicted. The character of the cerebral currents is changed, changes in higher nervous activity and changes in the blood (leucopenia, thrombocytopenia, etc.) occur. In particularly severe cases the latent stage may be absent and the primary stage may pass directly into the third stage.

In *the Third Stage of Pronounced Symptoms* (toxic or febrile period) all the typical features of radiation sickness are present: general malaise, fever, vomiting, diarrhea, hemorrhagic tendency, ulcerative processes in the digestive tract and hemorrhages in various organs. Gradually, septicemia develops and can prevail over the other signs. In this period the signs of myocardial involvement and involvement of parenchymatous organs are usually observed, in which degenerative and necrotic processes of varying severity usually develop. Among Japanese affected, the third period began approximately 10 days after the irradiation and lasted from several days to three weeks. This stage is concluded either with the death of the patient, or by a gradual, long-lasting fourth stage.

The Fourth Stage (recovery period), which lasts from several months to a year or more, is characterized by blood changes, functional or organic changes of the internal organs, metabolic disturbances and trophic diseases of the skin. This stage represents a peculiar, chronic form of radiation sickness. Thus, it may be said that the involvement of the heart and parenchymatous organs may be seen to varying degrees in the third and fourth periods of the acute form of radiation sickness and in most cases of the chronic form.

The respiratory organs (particularly the lungs) suffer relatively little in the acute form of radiation sickness. Only in a few cases are small hemorrhages seen. In those cases where more serious pathological changes are seen in the respiratory organs, they depend not so much on the radiation involvement itself as on the subsequent complications (e.g., septicemia). In the chronic form of radiation sickness, nonspecific chronic processes are often seen in the lungs in the form of pneumosclerosis and pleuropneumonias.

Frequently signs of shock in combined involvements can be seen even in the beginning of radiation sickness. It is reported that radiation involvements of the body are produced by products of protein decomposition formed through the influence of radiation. In radiation sickness there are found in the blood histamine-like agents capable of producing a fall in blood pressure, shock or syncope. Syncope with shock is seen in cases of early death from radiation sickness ("death in a flash"). Therefore, following the action of ionizing radiation, the body is predisposed to the development of shock. Even slight mechanical or thermal trauma in the presence of radiation sickness is often accompanied by a considerable decrease in blood pressure or even by the development of shock. This important fact should be kept in mind in operative procedures and in the selection of anesthesia for patients with combined trauma.

Effects of Activity and Drugs on Radiation Sickness

Existing data on the effect of physical rest or, conversely, on the effect of activity on the course of radiation sickness indicate that physical exertion induces it and that irradiated active animals die sooner and in a higher percentage than the same types of animals which have been in a state of physical rest. Experimental data presented with the clinical observations made on those affected by the atomic bomb explosion in Japan attest to the importance of physical rest for the wounded. Those afflicted with radiation sickness who were subjected to distant evacuation died sooner and in a greater percentage than those who were located near the provisional hospitals in the environs of Nagasaki. Evacuation is best accomplished before the development of the signs of radiation sickness.

Existing data permit us to believe that morphine does not exert any negative influence on radiation sickness, and in some cases even influences it favorably. Therefore, the use of morphine in combined trauma and as a preparatory measure for anesthesia and operation should be considered entirely feasible. A whole series of soporific agents can be used in radiation sickness, sometimes with a favorable influence on the course and outcome; for example, the bromides, Luminal and chloral hydrate. There are interesting data to the effect that during depression of the central nervous system, for example, by Luminal, a redistribution of radioactive agents occurs in the body, namely a decrease of them in the parenchymatous organs and an increase in the bones. Conversely, with excitation of the nervous system (Metrazol), the content of radioactive agents in the internal organs was increased. These data attest to the profound influence of narcotic agents on the distribution of radioactive agents in the body, and therefore on internal irradiation.

There are reports of a so-called protective action of atropine when given before irradiation. As reported, radiation sickness developed more slowly in the atropinized animals and their deaths occurred from much larger doses of X-rays than the deaths of the control animals.

This protective action of atropine is categorically denied by many authors. Nevertheless it is important to note the absence of any negative influence of atropine on radiation sickness, which makes it possible to use atropine in cases of combined involvements where necessary.

Anesthesia and Radiation Sickness

General Anesthesia.—The most common and widespread form of general anesthesia, particularly under conditions of military circumstances is still *inhalation anesthesia* (especially ether). During the Second World War it was used in 30.2 per cent of the cases, while during peace time it is used in almost 20 per cent of all cases of anesthesia. Experimental data indicate that irradiation with X-rays of animals which are anesthetized leads to weakening of the signs of the subsequent radiation sickness, lengthens the duration of life and decreases the mortality rate. Almost analogous data have been obtained through the use of alcohol anesthesia. Therefore, the use of narcotic agents before irradiation often exerts a definite protective effect against radiation sickness. The use of the same narcotic agents *after* irradiation no longer exerts a protective effect, and *does not* in any way *affect* the course and outcome of radiation sickness.

By using ether or certain other forms of anesthesia in those afflicted with combined trauma, motor excitation should be avoided and prevented in every way. Therefore, appropriate preparation for anesthesia (morphine injections, etc.) is needed, or else the use of ethyl chloride or other form of anesthesia is necessary, in which the stage of excitation is absent. Taking into account the clinical characteristics of the various forms and degrees of radiation sickness and of combined involvements and also the effect of narcotic agents on the respiratory, cardiovascular systems and the parenchymatous organs, it should be accepted that inhalation ether anesthesia may be used in the first and second periods of the acute form of radiation sickness and in the presence of mild chronic forms of it. In the third period of acute radiation sickness, and also in the moderate and severe degrees of chronic radiation sickness, inhalation ether anesthesia, as a rule, is contraindicated. The possibilities for use of ether anesthesia in wounded who are contaminated by radioactive agents depends on the presence and degree of the general signs, that is, in essence, on the signs of radiation sickness. If they are absent, any type of anesthesia may be used; if the signs of radiation sickness are present, then everything stated above applies to these cases. In those cases of combined involvements where ether anesthesia is contraindicated and inhalation anesthesia is necessary, recourse should be had (if working conditions permit) to safer *gas anesthesia* (nitrous oxide). The use of this technically complex form of anesthesia is possible, under conditions where atomic weapons are used, only at a great distance from the area of involvement.

Intravenous forms (hexanol, Evipan, Pentothal) of anesthesia are used as rarely in peace time circumstances (0.54 per cent in all anesthetics) as in war time (1.2 per cent). This is explained by the con-

siderable number of complications observed. Intravenous anesthesia not uncommonly produces a drop in blood pressure, which is lowered, even without this, in the majority of patients with combined involvements (traumatic or burn shock, hypotension from radiation sickness). Finally, it is known that intravenous forms of anesthesia are contraindicated in septicemia, peritonitis, severe hemorrhages, diseases of the liver and in very serious conditions of the wounded. Using sodium pentobarbital anesthesia, investigators performed operations (resection of small intestine) in irradiated dogs. In the operated dogs, the mortality rate was equal to 44 per cent; in the control dogs, 39 per cent, that is, there was a slight difference. In the operated dogs, the usual leucopenia following operation developed slowly, and on the second day after the operation even a leucocytosis was seen, whereas in the control animals at the same time the number of leucocytes dropped sharply (by 37 per cent). Other indices of the blood, body weight, general clinical and pathological picture of the radiation involvement in the operated dogs were no different in any respect. Neither anesthesia nor serious operation exerted any particular negative influence on the course and outcome of radiation sickness. These important observations certainly need further verification. Existing data permit us to believe that intravenous anesthesias may be used in the first and second periods of acute radiation sickness and in the presence of the mild forms of chronic radiation sickness. This type of anesthesia is contraindicated in the third period of acute and in moderate and severe degrees of chronic radiation sickness.

Rectal anesthesia (*Avertin, Narkolan*) is rarely used, and therefore we shall limit ourselves to only brief mention of it. If the necessity and possibility of using rectal anesthesia arises in cases of combined involvements, then everything which has been stated above with respect to intravenous anesthesia applies. In certain forms and degrees of radiation sickness various involvements of the intestine are seen. Thus, for example, in some persons who died following the atomic explosion in Japan, edema of the intestinal wall, necrosis of the glands and the formation of ulcers were seen in the large intestine. Sometimes, as early as the first period of development of radiation sickness, diarrhea was seen. Understandably, rectal narcosis is contraindicated in all these cases.

It is fitting to discuss the recent interesting experiments on the effect of anesthesia and hypothermia on the course and outcomes of radiation sickness. In 1942 it was shown in experiments on rats that marked refrigeration of the body before irradiation permits the survival of the rats even after large doses of X-rays. Magnesium sulfate was given and hypothermia was produced in irradiated animals; the refrigeration was accomplished before the irradiation, during it or immediately after it. It was clear that during refrigeration the mortality rate of the irradiated animals ranged from 62 to 73 per cent, while in the control animals, it ranged from 50 to 74 per cent. Thus,

hypothermia did not exert any negative influence on the length of life or the survival rate in radiation sickness. According to the experiments hypothermia (in combination with Nembutal anesthesia) decreased the radiosensitivity of rats, because in animals exposed to hypothermia, the mortality rate equalled 30 per cent while all the control animals died. These experiments on the use of anesthesia and hypothermia in radiation sickness are still few and, therefore, they do not permit us to draw any final conclusions.

Spinal anesthesia has not been extensively used either in peace time or in war time because of the definite technical complexity of it, requiring practice, and a relatively high frequency of various complications during and after its use. In peace time it was used in only 1.93 per cent of cases while during World War II it was used in 2.5 per cent of all cases of anesthesia. In the majority of combined involvements a drop in blood pressure is often seen. Spinal anesthesia itself also decreases the blood pressure considerably (20 millimeters and more) and for a long time (three to three and a half hours). Taking everything into account, spinal anesthesia in combined involvements, as a rule, is contraindicated.

It is not surprising that in peace time practice local anesthesia (especially, infiltration type) was used in 75 per cent and in World War II, in 65 per cent of all operations. Local anesthetic agents (especially, Novocaine) do not exert any kind of harmful general effect. Therefore, it may be considered that local anesthesia can be used in all cases of combined involvement. It is evidenced by experiments on animals and by certain clinical operations that local anesthesia can produce a favorable effect on the course and outcome of radiation sickness, while other experimental data deny any kind of protective properties of Novocaine to irradiation of animals by X-rays. However, Novocaine in these experiments did not exert any kind of negative influence on the radiation sickness. Taking into account the generally known merits of local anesthesia and the absence of any harmful effects of it in radiation sickness, local anesthesia should be considered the method of choice for anesthesia in those afflicted by combined trauma. Specifically, the use of local anesthesia in the treatment of wounds infected by radioactive agents facilitates the washing of these agents out of the tissues. Such wounds tend to develop suppurative infections and it is expedient to add antibiotics to the usual Novocaine solutions (penicillin, streptomycin). Experiments indicate that Novocaine solutions prepared with physiological solution do not affect the rate and character of absorption of certain radioactive agents from the subcutaneous tissues and muscles, while Novocaine solutions made from distilled water retard this absorption.

We have presented only the basic considerations and facts which might serve as a foundation for the selection of anesthesia in persons with combined radiation involvement. It is understood that this new and important topic is subject to further profound study.