Whole Body Hyperthermia at 43.5-44°C: Dream or Reality?
Alexey V. Suvernev, Georgy V. Ivanov, Anatoly V. Efremov and Roman Tchervov*

Abstract
A high level of body temperature (43°C) is needed for effective use of whole body hyperthermia. Such a high level hyperthermia can only be safely used taking into account a theory of developing post-aggressive hyperproteolysis. Besides the control of proteolysis, it is also necessary to apply total phentanyl anesthesia, high-frequency lung ventilation and a high rate of heating. Clinical application of this method allows inducing the apoptosis of malignant cells, decreasing the viral load in HIV and HCV-infected patients and also causing a general sanitary effect. Use of water immersion makes the technology noninvasive and "physiological". Application of this whole body hyperthermia technology reduces ventilation time and complications.

Introduction
It is known, that therapeutic opportunities of the thermal factor are used since ancient times. However, in the 20th century scientists and physicians have reached essential results in application of hyperthermia in treatment of oncological, immunological, viral and other diseases. Necessity of development and improvement of hyperthermic technologies was predetermined because of insufficient efficacy of commonly used surgical, pharmacological, immunobiological and other methods of treatment of dangerous (oncological, viral, immunological) diseases and detection of unknown clinical effects of a hyperthermia.

Those clinical significant effects are:
1. Destruction of malignant cells due to induction of necrobiosis and apoptosis by the thermal factor.
2. Elimination of tolerance of malignant cells to chemotherapy
3. Potentiation of medical effects of chemotherapy in combination with hyperthermia. It allows to reduce dosages of chemotherapy, decreasing damaging effect to the healthy tissues and keeping antineoplastic activity.
4. Activation of immunomodulating effects of hyperthermia, increase of protective forces of the patient, which important and never occurs after chemo- and radiotherapy.

Necessity of High-Level Whole Body Hyperthermia
It is known that there are no universal solutions for technical realization of artificial hyperthermia and for choosing its rational temperature range. Different variants of local and whole

*Corresponding Author: Roman Tchervov—Siberian Institute of Hyperthermia, Nagornaya 14a, Iskitim-5, 633205, Russia. Email: tchervov@inbox.ru.

body hyperthermia (wave, immersion and perfusional) should not be opposed to each other. It is necessary to take into account the concrete clinical situations to achieve the maximal medical effect.

Below we summarize arguments which were taken into account at studying and applying a high level (extreme) hyperthermia (up to 44.0°C).

First of all, it is important to reply: why is it necessary to achieve WBH above 43°C? The answer to this question is obvious not only for oncology, but also for those areas of medical practice where a selective cell damaging effect of heat is required. In particular, it is actual for oncological, virological and allergological practice, when it is necessary to initiate a necrobiosis and apoptosis of malignant cells, to suppress the HIV-infection or to destroy para-proteins and pathological antibodies.

Some inspiring results in this field have been already received. So E. Kano (1987) has established, that "... energy of activation of heat cell killing at temperatures from above 43.0°C and below 43.0°C is equal to 150 kcal/l and 360 kcal/l accordingly ..." Thus, on the one hand it is possible "to examine" an organism of the cancer patient protractedly on its nonspecific resistance to temperature up to 44°C during 1-3 hours per hope that cancer cells in his organism appear less steady against the increased temperature. On the other hand, in conditions of adequate anesthetic protection, rapidly provide the 43.0-43.5-44.0°C level of hyperthermia and to start the biological mechanism of apoptosis in cancer cells. We shall note, that doctor Kano with colleagues within the next 10 years repeatedly confirmed reliability of the phenomenon registered by them certainly accepted by us in attention. Also it is necessary to note, that Mathe G. on XXIVth Congress in Rome (September 2001) also has confirmed, that "... apoptosis of cancer cells is started only at achievement of temperature in 43.0°C ..."

The authority of these and other known scientists allows to consider that high level hyperthermia (above 43°C) is basic for oncological practice. Moreover, application of whole body hyperthermia in an interval of 40-42°C is fraught with a potential danger of dissemination of malignant cells and stimulation of their growth.

**Risk Factors of Whole Body Hyperthermia Over 43°C and Pathogenetic Substantiation of Their Overcoming**

It is known, that homoiothermic organisms "...are sheltered right at the threshold of thermal death..." Artificial realization of whole body hyperthermia even in an interval of 41.8-42.0°C is bound to the risk of development of dangerous complications. Those are:

- Thermal shock
- Brain edema
- Acute circulatory insufficiency
- Hepato-renal syndrome
- Acute respiratory distress syndrome (ARDS)
- Disseminated intravascular coagulation

The probability of occurrence of the specified complications is especially great in patients with oncological pathology; in elderly and senile age, when hyperthermia application is compelled on a background of multiple organ failure and the general bad state of health. In this connection at the 32nd Congress in Okayama (1994) it was noticed, that whole body hyperthermia up to 43°C is desired for clinical practice, but mortality reaches a level of 17%.

However our experience in whole body hyperthermia over 43°C with more than 500 patients, who successfully and repeatedly undergone this procedure with no complications and multiple organ failure, is a basis to assert about a basic opportunity of safe extreme hyperthermia.

Below there are some pathogenetic positions by which we were guided during development and perfection of high level whole body hyperthermia (43.5-44.0°C).