Translating Physiological Knowledge to Health Application

W. Selvamurthy and Shashi Bala Singh

Abstract

Physiology forms the basis for medical practice. Earlier in India, physiological research undertaken by medical teachers and researchers was primarily focused towards publications rather than translating that knowledge into a device/technology/process. The Defence Physiological Research and Development endeavours have provided a new paradigm since 1960 with the establishment of Defence Institute of Physiology and Allied Sciences (DIPAS). Most of the research efforts were aimed at finding solution to problems encountered by soldiers operating in extreme operational environments such as high-altitude, cold, desert, underwater and aerospace environments. Even the basic physiological research had an ultimate aim of application for the well-being of the soldiers thereby focusing on translational component. To cite a few examples, physiological responses during high-altitude acclimatisation studied on sojourners were translated to formulate the staging of acclimatisation schedule at high altitude. The nitric oxide and oxygen therapy for treatment of high-altitude pulmonary oedema (HAPO) resulted from the pathophysiological studies undertaken on the patients with HAPE. This resulted in devising an equipment to deliver a precise concentration of nitric oxide and oxygen to the patients while monitoring the concentration of nitrogen dioxide. Studies carried out to assess the physiological effects of heat stress resulted in formulating an ergogenic drink to keep the fluid electrolyte balance, thereby optimising the physical and mental efficiency of soldiers operating in desert environment. Development of a radio sensitiser, namely, 2-deoxy-D-glucose (2DG), came out of physiological research to find a method to ameliorate the adverse effects of radiotherapy in cancer patients. Such examples of translational research in physiology led to the development of products/technologies/processes which helped in providing health solutions which are illustrated in this chapter.

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Introduction

Integrated physiology has been in the forefront to facilitate the understanding of various functions of the organs and systems, which formed the basis of medical practice. Even the Nobel Prize in medicine is given as 'Physiology and Medicine' signifying the greater role of this discipline of medical sciences. Subsequently, physiology gave birth to many subset of disciplines such as molecular biology, genetics, etc. which have gained importance in the recent years. Physiological research in India in the early 1960s was primarily focused on the neurophysiology of food intake, sleep, consciousness, sensory physiology and respiratory functions [4, 34, 35, 37, 38, 43–48]. These led to the understanding of brain functions and other physiological systems. The clinical physiological research demonstrated the pathophysiological responses in different disease conditions [3, 5, 10, 25]. During the late 1960s, a new trend was set by the physiologists who focused on the applied and translational aspects of physiological research which benefited the soldiers and the society significantly. The establishment of Defence Institute of Physiology and Allied Sciences (DIPAS) as a part of Defence Research and Development Organisation (DRDO) was an important milestone to set the trend of translational research in physiology and allied sciences which enabled the soldiers to maintain optimal level of health and efficiency even in extremes of environmental and operational conditions while providing spinoff benefits to the society at large.

High-Altitude Physiology

The Indo-Chinese conflict in 1962 brought a concerted physiological research effort to understand human acclimatisation at high altitude (HA). The cardiovascular, respiratory, metabolic and neurophysiological responses during acclimatisation were studied on sojourners on acute induction and during prolonged stay at HA and compared with acclimatised low landers and high-altitude natives [22, 26, 41, 42, 49]. These endeavours ultimately resulted in the formulation of staging of acclimatisation [23]. If a soldier has to be inducted to extreme altitude (>5,000 m), he has to be taken through three levels of staging for better acclimatisation. The introduction of this staging procedure significantly reduced the mortality and morbidity and the operational efficiency of troops at HA.

High-Altitude Pulmonary Oedema

One of the serious clinical problems encountered among the sojourners at HA is high-altitude pulmonary oedema (HAPO). Increase in pulmonary hypertension, capillary permeability and decrease in surfactant were observed as the pathophysiological factors culminating in the development of HAPE [8, 33, 50]. Various hypotheses were promulgated to explain the pathophysiological mechanisms underlying the genesis of HAPE. These include transarterial leakage, exaggerated sympathetic nerve activity, J-receptor suppression, hypothalamic neurogenic mechanism, reduced chemoreceptor sensitivity and vascular and cerebrovascular water retention [21, 24, 28, 39, 53]. The introduction of diuretics resulted from studies on ADH and aldosterone leading to water retention which needs to be reduced for keeping the effective circulating blood volume at optimal level [12]. In view of hypobaric hypoxia being the important aetiological factor for the genesis of HAPO, a life-saving device, namely, HAPO bag (Fig. 1), that increases positive pressure simulating lower-altitude conditions was developed and supplied to large number of field stations over the Himalayas. This has resulted in saving a large number of lives which would have otherwise succumbed to HAPE [19]. Anand et al. demonstrated for the first time the application of nitric oxide (NO) at 15 ppm and oxygen (O_2) at 50 % concentration to be beneficial in the treatment of HAPE [1]. DIPAS scientist developed a device which can deliver precise concentration of NO and O_2 to the patients with HAPE while ensuring the safety of patients regarding elevated levels of nitrogen dioxide (NO_2) [11] (Fig. 2). A screening method

Fig. 1 HAPO bag

Fig. 2 Nitric oxide delivery system

to assess the susceptibility of individuals to develop HAPE was formulated using the exhaled NO measured by the chemiluminescence method [6]. This can be used to screen out susceptible individuals during rapid induction in emergency. In addition, a modified nebuliser was developed at the Institute of Nuclear Medicine and Allied Sciences (INMAS), another DRDO laboratory, to deliver pulmonary vasodilator drugs into the alveoli in nano size which has been successfully trial evaluated in HA regions [18].

Cold Injuries

Efforts were made to understand the aetiopathology and pathophysiology leading to various forms of cold injuries including frostbite which is the most severe form of cold injury. Subsequently, a new protocol for treatment using rewarming of the affected parts in tea decoction medium at temperature closed to body temperature and application of aloe vera cream was effective in

the treatment of frostbite [31]. A large number of aloe vera cream jars were distributed among the soldiers for both prophylactic and therapeutic applications (Fig. 3). Battery-operated heating gloves and socks were also developed to keep the extremities warm, thereby preventing frostbite (Fig. 4).

Fig. 3 Aloe vera cream

Oxygen-Enriched Shelter

Acute mountain sickness (AMS) is a common transient clinical problem manifested by headache, nausea, vomiting, sleep disturbance, loss of appetite, etc. These symptoms normally disappear after acclimatisation for a week [36]. However, severe cases of AMS need to be treated with administration of oxygen. In order to provide oxygen treatment to a large number of AMS patients, an oxygen-enriched shelter was developed and established in a few places at HA (Fig. 5). The solar energy was harnessed to light and heat the shelter [17].

Biodigester for Human Waste Management

Biodegradation of human waste is rather difficult in high altitude due to prevailing cold conditions in which microbes are unable to effectively

Fig. 4 Battery-operated socks and gloves

Fig. 5 Oxygen-enriched shelter

Fig. 6 Biodigester

biodegrade the constituents of the faecal matter. Scientists from Defence Research and Development Establishment (DRDE) collected a consortium of microbes from Antarctica, cultured them in the laboratory, studied their kinetics and developed a bioreactor providing a congenial medium and environment to produce a large quantity of this consortium. An underground structure to house these microbes was designed and developed which was linked to the superstructure of the toilet (Fig. 6). Since the consortium included bacteria which carried out the process of hydrolysis, acidogenesis, acetogenesis and methanogenesis and its high level of tolerance to cold and heat, these biodigesters are effective in a wide ranging environments from high altitude to desert [13]. These have already been installed in large number in Himalayan high-altitude regions, Lakshadweep Islands and in other parts of India.

Aerospace Physiology

The fighter aircrafts pose physiological challenges due to high G environment, hypoxia and explosive decompression during emergency ejections. G-induced loss of consciousness (G-LOC) and disorientation result in major air accidents. A sharp decline in cerebral perfusion due to blood pooling in lower extremities due to G force is the major factor responsible for G-LOC. Anti-G suit has been developed and introduced in Indian Air Force in large quantity. These clothing ensembles were made flame retardant [17].

Heat Acclimatisation

Environmental physiologists have evaluated the physiological effects of hot dry and hot humid environments on physical and cognitive functions [40]. This knowledge was translated to climatic mapping for various stations in hot humid and hot dry conditions prevailing across India for providing cooling and air conditioning in the zones of requirement [29]. Work–rest schedule of soldiers was formulated which minimised the incidence of heat casualties and improved work efficiency [2]. The fluid–electrolyte imbalance due to work in heat was mitigated by developing a suitable ergogenic beverage with potassium supplementation [30]. A thermoelectric cooling suit based on Peltier effect was developed and successfully demonstrated to have effective microclimatic cooling which could be worn by people working in high-temperature environments (Fig. 7).

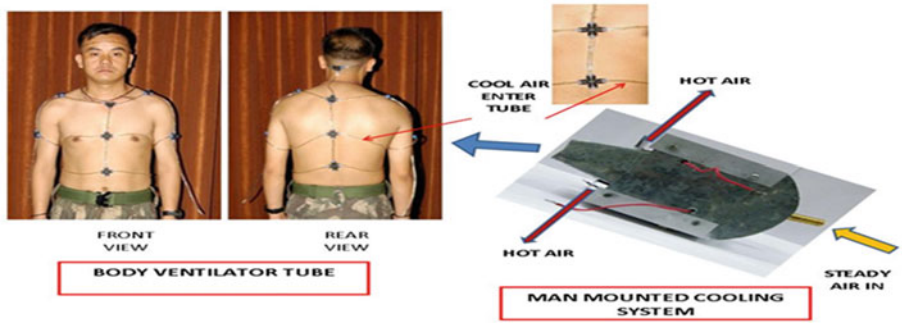

Fig. 7 Vortex cooling suit

Protection Against Noise-Induced Hearing Loss

Noise is a health hazard not only in military environments but also in industry, road traffic due to vehicular noise and even in living environments. Physiological research indicated the processes underlying temporary threshold shift (TTS) of hearing and permanent hearing loss (PHL) due to the damage of hair cells due to high-intensity noise. The conventional method of protection was by using barrier methods with the help of ear defenders such as ear plugs, ear muffs and active noise cancellation devices [9]. Scientists at DIPAS developed a novel approach using carbogen (5 % CO_2 and 95 % O_2) mixture to attenuate noise-induced TTS to protect from PHL. A mobile device was developed to facilitate carbogen breathing before and after noise exposure which resulted in significant protection against noise hazard [7] (Fig. 8).

Fig. 8 Portable carbogen breathing system

Underwater Physiology

Submarines operate at various depths under the sea in hyperbaric environments. In the event of submarine accidents, the crew need to escape from the submarine and pass through a gradual ascent to avoid decompression sickness and rapture of the lungs. An indigenous submarine escape hydro-suit along with the life support system for providing oxygen, nitrogen and helium was developed by the Defence Bioengineering and Electromedical Laboratory (DEBEL) and inducted in Indian Navy [27] (Fig. 9).

CBRN Defence Technology

Chemical, biological, radiological and nuclear (CBRN) threat is a global concern. A large number of protective devices have emerged from physiological and engineering innovation. Auto-jet injector is one such device which is used for administering atropine sulphate and PAM chloride for individual exposed to nerve agents.

Fig. 9 Submarine escape hydro-suit

These cholinesterase blocking agents protect neuromuscular transmission of impulses thereby protecting reversibly the individual exposed to nerve agents such as soman, sarine, VX and tabun [16, 52]. Efficient decorporating formulation using Prussian blue as the main ingredient has been developed and successfully trial evaluated for removing radionuclides ingested or inhaled [32]. A very innovative approach at INMAS to develop a radio sensitiser resulted in the formulation of 2-deoxy-D-glucose (2DG) which has completed phase III clinical trials successfully and ready to be launched for marketing. This can ameliorate the adverse effects of radiotherapy in cancer patients [14]. The radioprotective effect of Tulsi (Ocimum sanctum) was demonstrated and taken to phase II clinical trials.

Mosquito Repellent

Mosquitoes are the vectors for many diseases such as malaria, dengue and *chikungunya*.

Fig. 10 Herbal mosquito repellent

A tropical country like India provides congenial temperature, humidity and other environmental factors where mosquitoes can easily breed and transmit pathogens through biting either during the day or night. Mosquito repellents developed by DRDO provide long-lasting protection (8–10 h). These have been developed by undertaking the electrophysiological recording of antenogram of insects and testing the efficacy of different formulations having repellent properties [15] (Fig. 10).

Biomedical Technologies

Ambulatory physiological monitoring is required in many clinical as well as basic physiological research. However, to use such devices in difficult environments such as HA, desert, aerospace environment and Naval operational environments require adequate ruggardisation which has been accomplished by scientists at DEBEL [17]. A critical care ventilator was developed to provide optimal ventilation for patients in ICU and under critical care [51] (Fig. 11). Extensive research was carried out on a polyherbal preparation which was found to be very effective to treat leucoderma [20] (Fig. 12).

Fig. 11 Critical care ventilator

Fig. 12 Leukoskin

Conclusion

While basic research forms the foundation for seeding new technologies and generating new concepts and hypotheses, the applied research and its translations is vital to bring innovation to benefit the society at large. Translation from science to technology to product requires close interaction among three stakeholders, namely, academia, R&D institutions and industries. DRDO laboratories were able to successfully integrate these three entities which resulted in the development of a number of products, technologies, processes and solutions. Even the basic research conducted at our educational institutions and universities should be directed towards a specific goal or problem. Thus, the translational research in physiology or any other discipline will have greater impact on the welfare of the society, quality of life including health and generating wealth.

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