

History of thermal and environmental physiology in Japan: the heritage of Yas Kuno

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Dr. Yas Kuno was a pioneer in the field of sweat gland physiology. He trained many research scientists who formed the first generation of thermal physiologists. In turn, these investigators recruited qualified investigators, forming the second and third generations of thermal physiologists. At present, the third and fourth generations of investigators are actively engaged in research, expanding their interests to neurophysiology, chronobiology and exercise physiology.

Historical Background

The first scientific publication in the field of temperature regulation from Japan was *The Physiology of Human Perspiration*, published by Churchill in 1934 by Yas Kuno. An extended edition, titled *Human Perspiration*, was published as a monograph in American Lectures in Physiology by CC Thomas in 1956.

The first generation of thermal and environmental physiologists in Japan who worked together with Kuno include Korehiro Ogata, Shinji Itoh, Hisato Yoshimura, and Kentaro Takagi, as well as

Kokichi Ohara and Teruo Nakayama. Many students joined the laboratories run by that first generation, comprising the second generation of thermal and environmental physiologists in Japan. Furthermore, the students of the second generation form the third and fourth generations of thermal and environmental physiologists who are actively working at the present.

Avoiding sectionalism, Kuno stressed the importance of creative and cooperative research. He also felt it was important to share ideas and encourage each other through scientific meetings. His philosophy became a tradition that is now honored by Japanese physiologists in this field.

The following is a review of each of these generations of thermal and environmental physiologists in Japan, with emphasis on their cooperative works and the international meetings they organized.

The Legacy of Yas Kuno (1882–1977)

Yas Kuno was born on March 30, 1882, in Aichi Prefecture. After graduating from Aichi Medical School, the forerunner of the Nagoya University School of Medicine, he studied physiology at the University of Tokyo and then at Kyoto University until 1911, when he was appointed Professor of Physiology at Nannan Medical School of Medicine. In 1913, he went to Leipzig to study physiology and then moved to the University College London to study the physiology of circulation with Prof. Ernest Starling. After returning to Japan, he initiated his studies on the physiology of sweating, which became his life work. He noticed that heavy sweating in cold northern district leads to frostbite in the hands and feet. To analyze sweating mechanisms, he devised a new method for obtaining continuous measurements of the rate of

sweating from human skin. A celluloid dish attached to the skin was ventilated by dry air and connected to a U-tube filled with calcium chloride. Sweat from the skin was trapped by the U-tube, and the sweat rate was determined from the weight change of the U-tube measured every 5 minutes. Based on the systematic and extensive sweating activity measurements taken with this method, he classified sweating into 2 categories: “thermal sweating,” resulting from heat accumulation in the body, and “mental sweating,” stimulated by mental stress. He also studied the development of secretory activity in the sweat glands, together with their innervation and humoral control, as well as the physiological significance of thermal sweating in body temperature regulation. The results of those studies were published as *The Physiology of Human Perspiration*¹ in 1934.

In 1939, he assumed a post as a Professor of Physiology at Nagoya University School of Medicine, where he extended his work on sweating and covered further details of the sweating mechanism, including hemidrotic response, pulsatile secretion of sweating, the effects of thermal sweating on water and salt metabolism, and the related pathophysiology. The results of those studies were summarized in *Human Perspiration*² as a monograph in American Lectures in Physiology in 1956.

After retiring from Nagoya University in 1955, he continued his studies on human sweating at the Kyoto Prefectural University of Medicine. The final presentation of his life-long work was made into a special lecture titled *The Mechanism of Human Sweat Secretion* at the XXIII International Congress of Physiology in Tokyo in 1965. In that lecture, he presented a hypothesis that the neural control of human sweat apparatus has developed into cholinergic innervation from the adrenergic innervation of the sweat glands of primitive

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Table 1. Cooperative Research Projects on Thermal and Environmental Physiology in Japan

Years	Title	Organizer or Author
1946–1953	Physiological Response to Seasonal Variations	Y Kuno
1956–1958	Physiological Response to Cold Weather	Y Kuno
1956–1957	Disorders due to Cold Weather	H Yoshimura
1964–1965	Adaption to Climate	H Yoshimura
1966–1972	International Biological Program	H Yoshimura
1966–1972	Heat and Cold Tolerance	H Yoshimura
1966–1972	Adaptability of Ama (Diving women)	S Kobayashi
1969–1970	Circadian Rhythm	K Ogata
1973–1978	Central and Peripheral Adaptation to Temperature	K Ohara
1979–1981	Process of Adaptation to Heat and Cold	T Nakayama
1982–1984	Regulatory Mechanisms of Body Temperature	N Murakami
1986–1988	Heat Adaptation of the aged	T Ogawa
1988–1989	The Role of Bioactive Substances in Adaptation	T Hori
1990–1992	Analysis of Adaptation System	T Morimoto
1992–1994	Analysis of Factors to Modify Temperature Sensitivity	M Kosaka
1995–1998	Analysis of Sweating Mechanism during Heat Acclimatization	M Kosaka

animals to maintain cutaneous blood flow, avoiding adrenergic vasoconstriction.

In addition to these research activities, as a member of the Science Council of Japan, he presented a proposal to the Japanese Government for the promotion of cooperative research activities in various fields, and the Ministry of Education therefore organized a funding system for cooperative scientific research groups. Cooperative research activities summarized in **Table 1** were supported by the Ministry of Education, which contributed to the progress of research activities of this field over an extended time period.

The Japanese Journal of Physiology (renamed as the Journal of Physiological Science in 2006) was founded by Dr. Kuno in 1951, which he edited and published until 1970, when its publication was handed over to the Physiological Society of Japan. In recognition of his brilliant work, the Japanese Government awarded Dr. Kuno with the Academy Prize in 1941, followed by the highest decoration in the field of cultural achievements, the Order of Cultural Merits in 1963 and the Order of the Sacred Treasure in 1976. He was appointed as a member of the Japan Academy in 1949 and also received honorary memberships in the Physiological Society of Great Britain, the American Physiological Society and the Physiological Society of the Federal Republic of Germany.

In 1960, his students edited a book titled *Essential Problems in Climatic Physiology*³ as a tribute to Prof. Yas Kuno in celebration of his 77th birthday. This book covered “Physiological Responses to Heat” by S Itoh, “Physiological Responses to Cold” by K Ogata, and “Acclimatization to Heat and Cold,” including seasonal change in body fluid by H Yoshimura. “Problems Related to Thermal Regulation” were also dealt with, which included skin temperature, morphology of sweat glands, sex differences in sweating, axon-reflex sweating, shivering, the mechanism of hemi-hidrotic sweating, heat stroke, and the treatment of frostbite. **Figure 1** is a photo of Dr. Kuno from this book.

In 1972, a book titled *Advances in Climatic Physiology*⁴ was edited by his students in celebration of his 88th birthday, including contributions by Drs EF Adolph, J Achoff, DB Dill, OG Edholm, F Halberg, JD Hardy, SM Horvath, F Sargent, E Simon, M Smolensky, R Thauer, as well as contributions by the second and third generations of Japanese physiologists in this field.

Dr. Kuno passed away on December 30, 1977, and his contributions to the physiology of human perspiration stimulated the development of thermal and environmental physiology in Japan—in which his coworkers and pupils, including H Yoshimura, K Ogata, S Itoh, K Ohara, K Takagi and T Nakayama—played leading roles. Furthermore, the heritage of Dr Kuno has now descended to the present

generation of Japanese physiologists in this field. In **Table 2**, Japanese physiologists in this field are listed: Dr. Kuno’s students who formed the first generation are listed in the first line, and the second and third generations are shown in the lower cases.

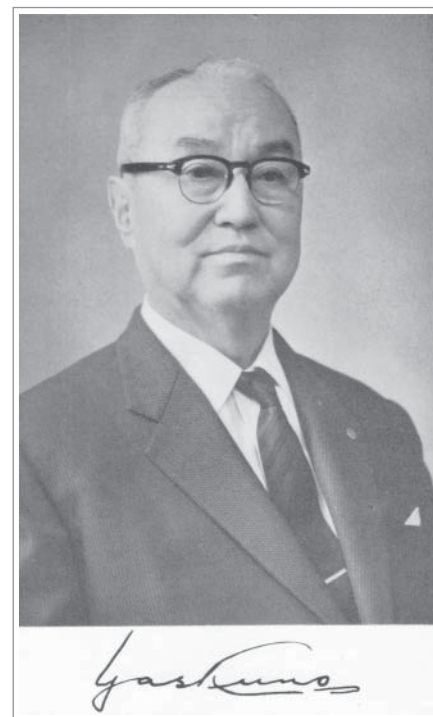


Figure 1. Yas Kuno. The phot is from the book “Essential Probles in Climatic. Physiology: A Tribute to Prof. Kuno in Celebration of his Seventy Seventh Birthday.” Edited by Y. Yoshimura et al., Nonkodo Publishing Co., Kyoto, 1960.

Table 2. Japanese Thermal and Environmental physiologists

K Ogata Kumamoto Univ	S Itoh Hokkaido Univ	H Yoshimura Kyoto Pref Univ Med	K Ohara Nagoya City Univ	T Nakayama Osaka Univ	K Takagi Nagoya Univ	Y Toda Kobe Univ	M Iriki Yamanashi Univ
T Sasaki	T Hiroshige	Y Toda	M Kosaka	T Hori	T Ogawa	T Araki	M Shibata
N Murakami	A Kuroshima	T Morimoto	Y Isobe	M Shibata*	J Sugeno*	Y Inoue	M Nagai
A Morimoto*	H. Ohinata*	H Nose*	H Satho	T Kiyohara*	T Nagasaka	N Kondo	S Nomoto
T Watanabe*	Y Agishi	A Takamata*	F Furuyama	S Aou*	O Shido*	M Shibasaki	M Hashimoto
	K Doi	S Nakai*		T Nakajima*	K Hirata*		
	K Honma	K Nagashima*		K Kanosue	S Sakurada*		
	S Homma	S Hori		K Matsumura	M Kosaka		
	K Moriya	K Shiraki		H Tanaka	T Matsumoto*		
		K Miki*		K Niwa	M Sugawara*		
		F Yamazaki*		Y Ohnuki	T Hori		
		K Yagita		T Midorikawa	K Nakamura		

*Indicates a student of the name above

Thermal and Environmental Physiology in Japan

Dr. Hisato Yoshimura (1907–1990) covered a wide range of research topics, including the acid-base balance of body fluid, protein nutrition, sport anemia, the cold induced vasodilation test, seasonal variations in body fluid and basal metabolism at Kyoto Prefectural University of Medicine. Dr. Yoshimura contributed greatly to organize cooperative research projects in the field of environmental physiology. He supported the projects conducted by Dr. Kuno as a manager and organizing many projects himself. In 1962, he was elected as the President of the Japanese Society of Biometeorology, which was founded by the first generation of thermal and environmental physiologists in Japan. In 1965, the International

Biological Program (IBP) was started, and he organized the International Symposium *Human Adaptability and its Methodology* in Kyoto (Fig. 2), and the result was compiled as the *IBP Handbook: Human Biology: A Guide to Field Methods*. As an organizer of the Human Adaptability section of the IBP in Japan, he recruited more than 100 scientists and led the project to great success during the period of 1966–1972.

Korehiro Ogata (1905–1979) worked together with Dr. Kuno at Nanman University as an Assistant Professor. In 1947, he became a Professor at Kumamoto University, where he worked on the seasonal variation of basal metabolism and circadian rhythm of body temperature with Dr. Takashi Sasaki, and thermoregulation and fever with Dr. Naotoshi Murakami. Dr. Murakami became a Professor

at Yamaguchi University, where he extended his work with Dr. Akio Morimoto and Dr. Tatsuo Watanabe. Unfortunately, Dr. A Morimoto passed away at the age of 39 (see Supplemental materials). Dr. T Watanabe is now working on the effect of angiotensin II and atrial natriuretic peptide on body temperature regulation as a Professor of Physiology at Tottori University.

Dr. S Itoh, Dr. K Ohara and T Nakayama worked with Dr. Kuno at Nagoya University. Dr. Shinji Itoh (1912–2003) moved to Hokkaido University, where Dr. Tsutomu Hiroshige, Dr. Kenichi Honma and Dr. Sato Honma did extensive work on chronobiology, while Dr. Akihiro Kuroshima and Dr. Katsuhiko Doi worked on BAT and non-shivering thermogenesis in relationship with cold tolerance.



Figure 2. International Symposium on Human Adaptability and its Methodology. By H Yoshimura at Kyoto, 1965.



Figure 3. International Symposium on Thermoregulatory Mechanism. By T Nakayama at Osaka, 1982.

Dr. Kokichi Ohara (1922–1986) studied physiology in the laboratory of Professor Kuno at Nagoya University. In 1957, he moved to Nagoya City University, and then he went to West Germany and studied the physiology of body temperature regulation in the laboratory of Prof. Thauer at the Max-Planck Institute. He visited Indiana University in 1964 and worked with Prof. Sid Robinson. He found that monkeys can sweat when they are exposed to heat repeatedly. He also succeeded in breeding a heat tolerant rat by successive crossbreeding, with Dr. F Furuyama.

Dr. Teruo Nakayama (1927–1989) joined Dr. Kuno's laboratory in 1950. He visited Dr. JD Hardy at the John Pierce Lab from 1960 to 1963 and found warm-sensitive neurons in the anterior hypothalamus. The results of his studies were reported in *Science* in 1961. Returning to Japan, he moved to Osaka University, where he extended his work together with Dr. Tetsuro Hori and with his students Dr. Kazuyuki Kanosue, Dr. Kiyoshi Matsumura and many other talented thermal physiologists. He edited many textbooks in the field of thermal physiology and played an important role in the progress of thermal physiology in Japan. In 1982, he organized an International Symposium on Temperature Regulation, as shown in **Figure 3**.

Dr. Nakayama passed away at the age of 62 (see Supplemental materials). Dr. Kentaro Takagi (1910–1990) was

appointed to the post of Professor of Physiology at Nagoya University after the retirement of Dr. Kuno. He studied the mechanism of hemihidrotic sweating. In that study, he found that during a period where pressure was applied on one side of the body, the sweat rate of oppressed side of the body was decreased, and the sweat rate of the other half of the body was doubled. Thereafter, he extended his studies to the mechanism of acupuncture. Many talented research scientists joined his lab, including Dr. T Ogawa, Dr. T Nagasaka, Dr. M Kosaka and Dr. T Hori.

Dr. Tokuo Ogawa visited Indiana University and worked on sweating activity devising continuous determination of sweating from a small area of skin with Prof. S Robinson and Prof. B Bullard using ventilation capsule and hygrometer. As a professor at Aichi Medical School, he extended his work on sweating with Dr. Masami Asayama and Dr. Junnichi Sugenoaya.

Dr. Tetsuo Nagasaka moved to Kanazawa University, where he worked on circulation and thermoregulation and also brain cooling with Dr. Osamu Shido and others. Dr. O Shido is now working on the central mechanism of heat acclimation as a Professor of Shimane University. In 2009, he sponsored the 3rd International Symposium on Physiology and Pharmacology of Temperature Regulation, with many participants from all over the world (**Fig. 4**).

Dr. Mitsuo Kosaka became a professor at Nagasaki University, where he worked on heat shock proteins and ethnic difference of sweating activity with Dr. Takaaki Matsumoto. Dr. Tetsuro Hori worked extensively on the central mechanisms of thermoregulation, especially hypothalamic neurons with Dr. Nakayama at Osaka University. Later, he assumed a post as a professor at Saga University and continued his work with Drs. Masaki Shibata, Toshikazu Kiyohara and Toshihiro Nakashima, and then at Kyushu University with Shuji Aou. Dr. T Hori passed away in 2009, and Dr. Blatteis contributed a reminiscence of Dr. Hori to Fever Lab. net.

In April of 2015, Nagoya University appointed Dr. Kazuhiro Nakamura as the Professor of Physiology, where he is working on the neural network of thermoregulation. Thus, the long history and traditions inspired by Dr. Kuno in the field of thermal physiology have been revived at Nagoya University.

Dr. Yoshiaki Toda (1915–1989), after studying in Kyoto with Dr. H Yoshimura, moved to Kobe University as a Professor. At his Lab, Dr. Yoshimitsu Inoue, now working at Osaka International University, studied the development of sweating activity during childhood and deterioration of sweating activity with aging.

Dr. Masami Iriki graduated Tokyo University, and he later went to West

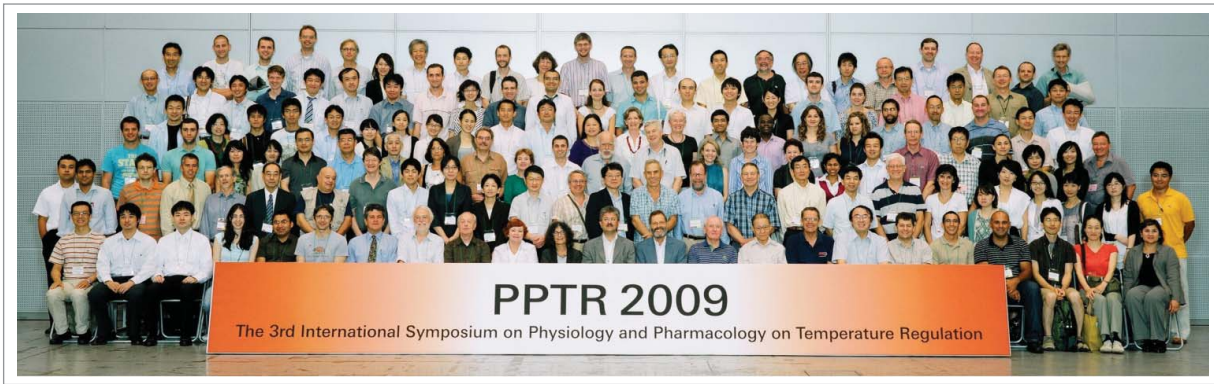


Figure 4. International Symposium on Physiology and Pharmacology of Temperature. Regulation. By O. Shido at Izumo, 2009.



Figure 5. Man in Stressful Environment, Thermal and Work Physiology. By K Shiraki at Kitakyushu, 1986.

Germany and studied the physiology of body temperature regulation in the laboratory of Prof. R Thauer, as well as with Prof. E Simon at the Max-Planck Institute. Returning to Japan, he became a Professor of Yamanashi Medical School, where he studied fever syndrome,

endogenous pyrogen and other subjects with Dr. Masaaki Hashimoto and other coworkers.

At the laboratory of Dr. H Yoshimura at Kyoto, Dr. Seiki Hori worked on the adaptation to hot climate and the assessment of heat tolerance. Later, he

continued his work at Hyogo Medical School. Dr. Keizo Shiraki studied sports anemia and extended his work to diving physiology later at the University of Occupational and Environmental Health in Kitakyushu. In 1986, he organized the International Symposium on Physiology

Table 3. Publications and the International Symposium on Thermal and Environmental Physiology

Years	Title	Organizer or Author
1934	The Physiology of Human Perspiration (Monograph)	Y Kuno
1956	Human Perspiration (Monograph)	Y Kuno
1960	Essential Problems in Climatic Physiology (Publication)	H Yoshimura, K Ogata, S Itoh
1965	Human Adaptability and its Methodology (Symposium)	H Yoshimura, JS Weiner
1972	Advances in Climatic Physiology ((Publication)	S Itho, K Ogata, H Yoshimura
1975	Physiolofy of Cold Adapted Man (Monograph)	S Itoh
1982	International Symposium on Thermoregulatory Mechanism (Symposium)	T Nakayama
1983	Hyperbaric Medicine and Underwater Physiology (Symposium)	K Shiraki, S Matsuoka
1984	International Symposium on Chronobiology (Symposium)	T Morimoto
1986	Man in Stressful Environment, Thermal and Work Physiology (Symposium)	K Shiraki, MK Yousef
1987	Man in Stressful Environment, Thermal and Work Physiology (Publication)	K Shiraki, MK Yousef
1992	International Symposium on Space Medicine in Nagoya 1992 (Symposium)	N Matsui
1995	Body Temperature and Metabolism (Symposium)	T Nagasaka, AS Milton
1997	Nagano Symposium on Sports Sciences (Symposium)	H Nose, ER Nadel, T Morimoto
1999	Exercise, Nutrition, and Environmental Stress (Symposium)	H Nose, CV Gisolfi, K Imaizumi
2000	Exercise, Nutrition, and Environmental Stress (Symposium)	H Nose, LL Sprit, K Imaizumi
2009	International Symposium on Physiology and Pharmacology of Temperature Regulation (Symposium)	O Shido

of Stressful Environment (Fig. 5) and the proceedings were published as *Man in Stressful Environments, Thermal and Work Physiology*.⁵ This book was edited as a tribute to Professor Hisato Yoshimura in celebration of his 77th birthday.

Succeeding Dr. H Yoshimura, Dr. Taketoshi Morimoto worked on the effect of dehydration on thermoregulation with Dr. Hiroshi Nose, Professor of Shinshu University, and other coworkers, and he elucidated the mechanism of voluntary dehydration after sweating, which was first reported in the classical book by Dr. EF Adolph, *The Physiology of Man in the Desert*. Dr. Seiichi Nakai conducted an epidemiological survey of heat stroke casualties in Japan and actively worked for the prevention of heat stroke casualties.

At present, Dr. Kazuhiro Yagita, Professor of Physiology at Kyoto Prefectural University of Medicine, is working on circadian rhythm. Dr. Yagita's group found a clock

gene in peripheral cells, and they are now working on the mechanism of circadian clock development in mammalian cells.

Some of publications and the international meetings related to thermal and environmental physiology held in Japan are listed in Table 3.

Cooperation by thermal and environmental physiologists in Japan continues even today. In 1996, the Environmental Physiology Section of the Physiological Society of Japan instituted the Yas Kuno Memorial Award for Young Investigators.

In addition, the heat wave attack is increasing due to global warming and the incidence of heat stroke is also increasing. For the prevention of heat stroke death, we edited *A Guidebook for the Prevention of Heatstroke during Sports Activity*, and also *Every Day Activity*. Many of the thermal and environmental physiologists in Japan previously listed participate in projects to prevent heat stroke casualties.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Supplemental Material

Supplemental data for this article can be accessed on the publisher's website.

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