Temperature 1:1, 6–11; April/May/June 2014; © 2014 Landes Bioscience

The legacy of Carl Vincent Gisolfi in temperature regulation

Charles M Tipton[1,*] and Kevin C Kregel[2]

[1]Department of Physiology; University of Arizona; Tucson, AZ USA; [2]Department of Health and Human Physiology; University of Iowa; Iowa City, IA USA

Carl Vincent Gisolfi (1942–2008) was a Distinguished Professor of Exercise Science at the University of Iowa whose contributions included mentoring future investigators and seminalstudies in the areas of thermoregulation during exercise, responses of the diencephalon to elevated temperatures, fluid absorption during heat stress, and the role of heat shock proteins in circulatory failure.

Introduction and Background

We commend Editor-in-Chief Romanovsky for (a) promoting feature sections devoted to history and (b) recommending we acquaint readers with the career and accomplishments of the late Carl V Gisolfi (1942–2000). He was such a revered faculty member at the University of Iowa that the administration lowered the American flag to half-mast on the day of his death, June 3rd, 2000 (**Fig. 1**).

In 1942, Carl was born on November 15 to his proud parents, Jean and Hugo Gisolfi, in the Bronx district of New York. Later his family was increased by the addition of sister Antonia and brother Gerald. Both his grandfather, an immigrant from southern Italy, and father had responsible positions in the New York garment industry. After completing elementary and middle school education in Bronxville, NY, the family moved to Tuckahoe, NY where Carl enrolled at Roosevelt High School and became renowned for his athletic ability in track and football. It was here he met the attractive and intelligent Louise Patrash who later became his wife and "best friend" (**Fig. 2**).

In 1960 he enrolled in Manhattan College where he majored in the biological sciences with an emphasis in physiology, excelled on the track team, and graduated 4 y later with a BS degree with Praise. A year later, he married his "best friend" and started a family that resulted in 3 healthy and talented daughters: Kristen, Tanya, and Nicole. Subsequently, he was admitted to the graduate program in physiology at Indiana University (IU) in Bloomington, IN where he was awarded a pre-doctoral fellowship that enabled him to be selected by Professor Sid Robinson (1902–1982) to become his first PhD candidate.

The relationship between Robinson and Gisolfi was a lasting one of mutual admiration and respect (**Fig. 3**), as Robinson also had an impressive list of credentials that included being the first PhD candidate of the late Dr D Bruce Dill at the Harvard Fatigue Laboratory who was also a premier scientist with a dedicated interest in the physiology of running and the production of heat. In addition, Sid Robinson was a middle distant runner who represented the United States in the 1928 Olympics. Thus, it was no surprise that his PhD thesis at IU pertained to the physiological effects of exercise which resulted in 2 publications in the *Journal of Applied Physiology* (JAP),[1,2] a journal published by the American Physiological Society (APS).

After receiving a PhD degree in physiology from IU in 1969, he accepted an academic appointment as an Instructor in the departments of Physiology and Biophysics and Physical Education–Men (Later changed to Exercise Science) at the University of Iowa (UI) located in Iowa City, IA. Later, he advanced in rank in both departments with appointments in 1972, 1975, and during 1981 before emerging as a full Professor. In 1996, he was appointed by the university as a Distinguished Professor of Exercise Science.

Figure 1. The lowering of the American Flag to half-mast at the University of Iowa Hospital Complex on June 3rd, 2000 to acknowledge the untimely death of Carl V Gisolfi. Seated below were 3 of his 6 grandchildren. Courtesy of Louise Patrash Gisolfi.

Teaching and Mentoring Contributions

In his 31-year tenure at the UI, he had extensive teaching responsibilities in both departments that involved 14 different courses. All were physiological in nature and pertained to aspects of human, medical, mammalian, exercise, and environmental physiology for undergraduate, graduate, nursing, medical, physician assistant, and teacher certification students. Classes were offered during both semesters, during the summer, and on weekends for certification purposes. Class size ranged from 5 to 300

Keywords: Carl V Gisolfi, thermoregulation, innovative scientist, effective administrator, dynamic leader, innovative and classic thermoregulatory study

*Correspondence to: Charles M Tipton; Email: tipton@email.arizona.edu

Submitted: 03/19/2014

Revised: 04/17/2014

Accepted: 04/17/2014

Published Online: 04/29/2014

http://dx.doi.org/10.4161/temp.29005

Figure 2. Carl V Gisolfi and his "best friend" and wife, Louise Patrash Gisolfi, at the 1985 American College of Sports Medicine (ACSM) banquet when he was elected President of the Society. Courtesy of Louise Patrash Gisolfi.

Figure 3. A 1969 photograph of Carl V Gisolfi and his mentor, the late Professor Sid Robinson of Indiana University. Courtesy of Louise Patrash Gisolfi.

individuals with the majority being team taught (and frequently included Charles M Tipton). However, several became his sole responsibility (e.g., exercise physiology, environmental physiology, scientific foundations of conditioning, and physiology for physician assistants). Gisolfi was an immaculately dressed, well prepared, and effective teacher who was both popular and admired by students, especially those in the College of Nursing. In fact, Tipton avoided being around Gisolfi after his lectures to the nursing students because he (Tipton) instantly became an invisible physiologist. It is noteworthy the College of Medicine in 1975 recognized him as The Teacher of the Year. Several years after his arrival at UI, he became a key contributor to the federally funded Interdisciplinary Exercise Science Training Grants awarded to Tipton and co-taught courses for students enrolled within the program (**Fig.** 4). Because of his knowledge, caring attitude, and infectious personality, he was a magnet for students and mentored 10 PhD students and started the process with 5 others before his untimely death (**Table 1**). In addition, he mentored 7 MS candidates, 28 undergraduate students, and 4 individuals who left his laboratory to enter medical schools . Gisolfi was especially proud of mentoring undergraduate students and frequently reminded Tipton he was following the tradition established by the Harvard Fatigue Laboratory of inviting undergraduates to assist in laboratory research projects. Like Robinson, he was proud of his track heritage (he was the "anchor leg" of the Manhattan College track team) and accepted (and won) every 440 yd challenge from graduate students who had "lettered" in track at their representative institutions. Regardless, all who left his laboratory were enriched by the experience, his knowledge, and his concern for their future.

Research Contributions to Temperature Regulation

Overview

Because of his research potential in the areas of exercise and temperature regulation, Gisolfi was recruited to the UI campus in the fall of 1969. After his arrival,

he had a climatically controlled environmental chamber (similar to one at Indiana University) constructed in his exercise physiology laboratory that contained a treadmill and features suitable for temperature regulation studies in humans. Later, he developed adjacent facilities suitable for thermal investigations with primates and rodents. Following in the footsteps of Dill and Robinson, he was a "master" in analyzing expired air gas samples by the Van Slyke procedure.

Besides his PhD thesis, Gisolfi was associated with 2 publications from his pre-doctoral years[3,4] plus 159 publications at the UI (Web of Science). Among this listing were 4 manuscripts in the Classic Category (cited more than 100 times in peer reviewed journals) and 1 that was selected by the Editor-In-Chief (Elsworth Buskirk, 1970–1974) of *Medicine and Science in Sports* (MSS) as the most important Journal article published during his tenure.[5] In addition, he wrote 10 chapters and 1 book (**Fig. 5B**). In addition, his laboratory received collectively approximately

Figure 4. Photograph taken during late 1970s and early 1980s of students associated with the laboratories of Charles M Tipton and Carl V Gisolfi while participating in the Interdisciplinary Exercise Science Graduate Program . Individuals shown are: front row (L–R): R Oppliger, T Bedford; second row (L–R): C Gisolfi, S Brown, P Kershner, J Fruth, K Rowlett, C Tipton; third row (L–R): J Christman, W Mitchell (technician), L Louters, K Marcus, T Wall.

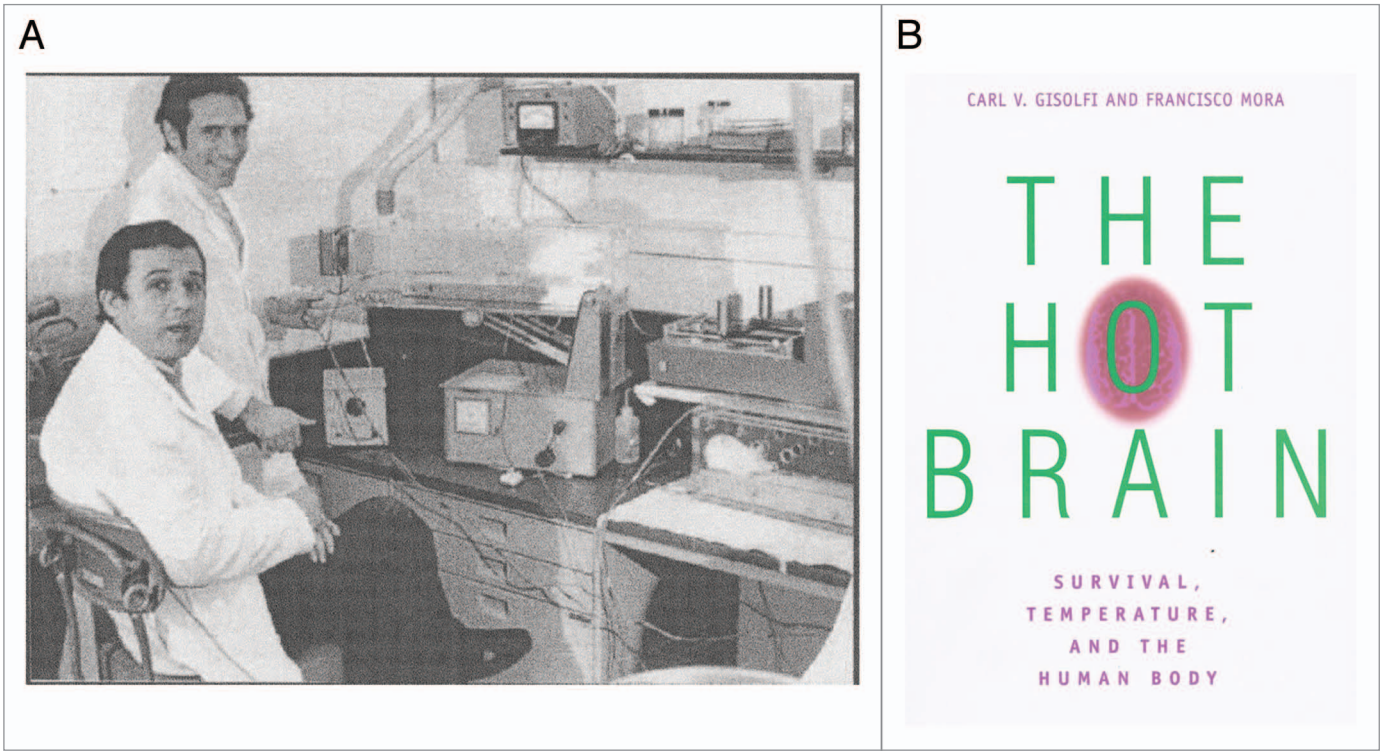

Figure 5. (**A**) Professors Carl Vincent Gisolfi and Frank Mora conducting an infusion study with exercising rats using the animal treadmill developed by Toby B Bedford, Charles M Tipton, Carl V Gisolfi, and associates.[6] Courtesy of Kevin C Kregel. (**B**) Cover of the text, *The Hot Brain* (The MIT Press), co-authored by Carl V Gisolfi and Frank Mora and published after the death of Carl V Gisolfi.

Table 1. PhD Students of Carl Vincent Gisolfi.

Student's name	Year graduated	Current position
John V. Christman	1983	Developed PowerPosture Program
P. Tim Wall	1987	Physical Therapist, Little Rock, AR
Kevin C. Kregel	1987	Professor & DEO, University of Iowa, Health & Human Physiology
Mallard D. Owen	1987	Vice President, Business Performance Services, Lindsey Business Group and Co-Owner, Inner Circle of Northern Virginia
Michael J. Kenney	1988	Professor & Head, Department of Anatomy and Physiology, Director of the Veterinary Biomedical Sciences Graduate Program, Kansas State University, Manhattan, KS
Alan J. Ryan	1992	Assistant Research Scientist/Engin, Internal Medicine, University of Iowa, Iowa City
Xiaocai Shi	1994	Founder of Sports NutriLight, Inc., greater Chicago Area
Shawn Flanagan	1996	Lecturer, Health & Human Physiology, University of Iowa
Ray Tai Chang	1996	Professor, National Taiwan University, Dept of Physical Education, Kaohsiung City, Taiwan
Dave Hall	1997	Lecturer, Human Anatomy & Physiology, Kirkwood Community College, Iowa City
Robin Looft-Wilson	2000	Associate Professor, Dept of Kinesiology & Health Sciences, The College of William & Mary
Douglas G. Whyte	2004	Senior Lecturer, Australian Catholic University, School of Exercise Science
Jennifer Rogers	2003	Lecturer, Health & Human Physiology, University of Iowa, Iowa City, IUA
Pat Lambert	2001	Associate Professor, Department of Exercise Science, Creighton University, Omaha, NE
Jo Morrison	2004	Assistant Professor, Longwood University, Health, Athletic Training, Recreation & Kinesiology, Farmville, VA

Students highlighted in gray are those that started out with Dr. Gisolfi, but received degree after his death under the direction of another individual.

7.5 million dollars in research funds from 4 federal agencies (NIH, ONR, NASA, DOD), 3 private corporations (Quaker Oats, Ross Laboratories, Hoffman-Roche), the NCAA, and from US Cycling. In keeping with the mandate from the Editor-In-Chief, general comments will be made highlighting Gisolfi's research endeavors, whereas specific information will be provided pertaining to his significant research contributions in the fields of thermoregulation, exercise, and human performance.

The initial decade (1969–1979)

During the early stages of his career at the UI, Gisolfi devoted an inordinate amount of time to the procurement of research funds and to the construction of his research laboratory. Once these tasks were completed, he initiated a series of human investigations that included the assessment of changes in 2–3 DPG levels in exercising children; work-heat tolerance relationships in distance runners who followed interval training; mean skin changes during exercise; intermittent work and thermal responses, and the balancing of electrolytes and fluid loss in thermal stress. The background for the study identified by MSS was the classic desert of Pitts and associates (AJP 142:253, 1944) in which the rise in rectal temperature was closely related to the percentage of water lost. With the Gisolfi and Copping investigation, subjects exercised at 75% VO_2 max in the heat (33.5/21.5 °C, dry/wet bulb). They found cold or warm replacement water had no influence on the value of replacement; the consumption of fluid during a run was more effective in reducing the rise in rectal temperature than consuming a similar volume 30 min before the run began, and "sponging off" with a cold wet towel was ineffective in preventing a rise in rectal temperature.[5]

During this time interval, he began investigations with animals and collaborated with Professors Myers at Purdue University, Mora from the University of Complutense in Madrid, Spain (**Fig. 5A**), and Professors Farber, Phillips, and Tipton at UI. Years later, Mora co-authored with Gisolfi the text entitled the *Hot Brain* (**Fig. 5B**).

His laboratory developed an apparatus for measuring oxygen consumption of exercising primates with the intent to determine the role of calcium (and its inhibitors) on temperature regulation during exercise. They subsequently infused different concentrations into the diencephalic regions to evaluate changes in colonic and hypothalamic temperatures and reported elevated concentrations of calcium within the hypothalamus did reduce elevated colonic temperatures in both primates and rats. With Toby Bedford, Charles Tipton and others, he helped perfect the development of a rodent treadmill, finalize a standardized exercise protocol, evaluate VO_2 max response, and publish results demonstrating a training effect had occurred.[6] The methodology from this article became one of the most followed by members of the exercise research community that used rats in their experiments.

The middle decade (1980–1990)

This productive decade was associated with 30 published investigations with the majority involving animals. The human studies addressed the role of interval training on the heat tolerance of young women; left ventricular functioning of cyclists; sweating responses of a hyperdidrotic patient; gastric emptying while exercising in the heat; and the controversy of whether a carbohydrate-electrolyte (CHO-E) beverage or water (H_2O) was better when exercising in the heat.

The extensive and impressive animal investigations featured injections and infusions of substances into either the circulation or brain that were known, or speculated, to modulate temperature responses. These substances were apomorphine, pimozide, norepinephrine, dopamine, DAME, select opiates, angiotensin II, and arginine vasopressin. However,

one animal investigation accorded the "Classic" status was by Kregel and associates.[7] After rats were implanted with Doppler flow probes on arteries in 4 different vascular beds, they were exposed to heat loads which progressively elevated mean blood pressure (MBP), heart rate (HR), core temperature (T_C), and vascular resistance (VR). They observed an increase in MBP until T_c reached approximately 41.5 °C, at which time MBP fell precipitiously to hypotensive levels. Of note was VR increased early in the mesenteric bed with the heat load before exhibiting a continuous decrease that occurred approximately 10–15 min before the dramatic decline in MBP. They theorized a selective loss of compensatory splanchnic vasoconstriction had occurred which triggered the cascade of physiological events that characterize heat stroke.[7]

Figure 6. Three former ACSM presidents at the 1998 convention. (L–R): Charles M Tipton (1974–1975), Barbara L Drinkwater (1988–1989), and Carl Vincent Gisolfi (1985–1986). Courtesy of Barbara L Drinkwater.

The final years (1990–2000+)

Despite being diagnosed with a fatal disease in 1991 (of which he never complained or indulged in self pity), this decade was his most productive as demonstrated by 49 publications and the receipt of 89% of his total funding from external sources. Highlights of his human research included: 1) the demonstration that measurements from the tympanic membrane could be used to assess core temperature, 2) the first studies demonstrating that humans produce heat shock proteins (HSP) when exercising in the heat and HSP-70 was a useful marker for thermal tolerance (in collaboration with Pope Mosely), and 3) seminal clinical investigations with faculty from the UI Department of Internal Medicine on gastrointestinal (GI) function and fluid absorption. These collaborative studies included the examination of consumption and absorption of carbonated and non-carbonated beverages on GI function and performance; the role of osmolality and sodium concentration on fluid consumption in the heat when exercising; gastric emptying, motor activity, and intestinal absorption during exercise in the heat; the effect of aspirin on intestinal permeability; the impact of graded exercise on colonic and esophageal motility; gastresophageal reflux in trained subjects, and the intestinal permeability of runners after the 1996 Chicago marathon. In addition, he conducted a study for the NCAA to determine the merits of blood and urine measures to assess the dehydration status of athletes. Although the urine measures (urine specific gravity and osmolality) were of minimal value, plasma osmolality levels were helpful for this purpose.

Highlighted animal investigations included rat mesenteric artery function after hind limb suspension; responses of eccrine sweat glands of patas monkeys to acclimation; intestinal perfusion of protamine and paracellular transport of water and carbohydrates; splanchnic sympathetic nerve responses with hyperthermia; heat stress, HSPs and endotoxin shock; hypoxia in splanchnic tissues; and the potential role of heat acclimation on rat mesenteric artery responses to norepinephrine.

Two publications on animals received the "Classic" status. The first was by Ryan et al. and related to the cross-resistant relationship between heat stress and endotoxin shock.[8]

Knowing bacterial lipopolysaccharide (LPS) had a potentially lethal in vivo effect, they designed a study in which 4 groups of rat received either saline injections and no heat stress, LPS injections, heat stressed (47–50 °C) with LPS injections, and saline injections with heat stress. A 24 h period existed between the heat stress and the injections. While the rise in T_c was similar in all groups, the 48 h survival rates were distinct, as the majority of rats in the LPS treated group (no heat stress) did not survive. On the other hand, all animals subjected to the heat stress protocol before the LPS injections survived. Hence, they concluded an acute heat stress exposure can provide protection against the lethal action of LPS (and inferring the protective process involved an immune component).[8]

The second study of note was by Hall et al. and pertained to the influence of hyperthermia on the formation of reactive oxygen species (ROS) and the role of nitric oxide in the process.[9] This technically difficult set of experiment required heat stress, electron paramagnetic spectroscopy, sampling of blood samples from the portal vein and femoral artery, detecting the presence of radicals and metal binding proteins, and relating changes to rectal temperatures of rats. From their results, the Gisolfi team concluded it was the first demonstration that "whole body hyperthermia produces

increased concentrations of radicals and metal binding proteins in the venous blood of the rats and suggests severe hyperthermia stimulates an enhanced local release of nitric oxide within the splanchnic circulation".[9]

Recognition and Honors

Early in his career he was recognized for his physiological knowledge concerning temperature regulation by being a reviewer for 10 different professional journals; appointed to the Editorial Boards of the JAP, MSSEX, and the *International Journal of Sports Nutrition;* becoming an Associate Editor for JAP and MSSEX, and the lead Editor for 5 volumes of the series entitled *Perspectives in Exercise Science and Sport Medicine* that was initiated by the Gatorade Institute of Exercise and Sport Sciences. Additionally, he served on 2 NIH Study Sections and as an expert on site visit panels organized by NIH, DOD, and the National Academy of Sciences. His leadership ability was quickly noticed by APS who appointed him as member and chair of several important committees including the Section Advisory Committee which organizes the APS program for the yearly Experimental Biology Meeting. He subsequently was elected APS Chair of the Environmental and Exercise Physiology Section (EEP) and initiated a fund raising drive that ultimately resulted in the EEP Section providing more student awards than any of the other APS sections. In 2000, the EEP Section selected him to present the prestigious Edward F. Adolph Lecture Distinguished Lecture at its next annual meeting. Unfortunately, he died before the meeting was held. Previously, he had received 125 invitations to present seminars or lectures from universities, institutes, agencies, and various groups from 25 States and 9 foreign countries.

He received numerous awards and honors that included fellowship, a Citation Award, an Honor Award, and a Presidency (**Fig. 6**) from ACSM and the ACSM Foundation; an Honor Award from the EEP Section of APS; fellowship from the National Academy of Kinesiology, and a Distinguished Service Award from the Department of Physical Education and Human Performance of Manhattan College in 1995.

Closing Comment

Carl Vincent Gisolfi was a unique human being with many talents and attributes who made a difference in the lives of many individuals who had the pleasure of meeting and knowing him. He will be greatly missed by all.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

It is a pleasure to acknowledge Dr Toby B Bedford, Joan Seye, and Paula Wallin Tipton for their assistance in finalizing this manuscript.

References

1. GisolfiC, et al. J Appl Physiol 1970; 29:368-73; PMID:5451314
2. GisolfiC, et al. J Appl Physiol 1970; 29:761-8; PMID:5485343
3. GisolfiC, et al. J Appl Physiol 1966; 21:1767-72; PMID:5929302
4. GisolfiC, et al. J Appl Physiol 1969; 26:530-4; PMID:5781602
5. GisolfiCV, et al.Med Sci Sports 1974; 6:108-13; PMID:4461967
6. BedfordTG, et al. J Appl Physiol Respir Environ Exerc Physiol 1979; 47:1278-83; PMID:536299
7. KregelKC, et al. J Appl Physiol 1985; 64:2582-8; PMID:3403442
8. RyanAJ, et al. J Appl Physiol 1985; 73:1517-22;PMID:1447099
9. HallDM, et al. J Appl Physiol 1985; 77:548-53;PMID:8002499