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HISTORICAL PERSPECTIVES ON CARDIOVASCULAR RESEARCH UNDER MICRO-G CONDITIONS

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ABSTRACT

In this article the early beginnings of space physiology are briefly reported based upon personal communications and on other reports and publications not currently easily available. Space physiology has evolved from hypergravity experiments. It originally was the aim in centrifuge laboratories to study the limits of g-tolerance. Instead of forward extrapolations from data derived from hypergravity experiments, in 1945–1947 Gauer and Haber extrapolated downwards to zero-g and came to astonishingly precise predictions of what might happen to the human physiology when man entered a zero-g environment. The article under the title "Man under gravity-free conditions" published in German Aviation Medicine World War II Volume 1: 641–644 was the first scientific article laying the basis for further developments in space medicine. This article must be regarded as the beginnings of space physiology. From then on, the manipulation of gravity became a tool for physiologists. In the present article, the developments during the pre-war period in Berlin and the USA will be outlined briefly and some of the pioneers in this field mentioned.

Keywords: *hypergravity, g-tolerance, high-g laboratories, operation paper clip*

ZGODOVINSKI VIDIKI RAZISKOVANJA SRČNO-ŽILNEGA SISTEMA V MIKROGRAVITACIJSKIH POGOJIH

IZVLEČEK

Ta prispevek opisuje začetke vesoljske fiziologije na podlagi osebnih pričevanj in ostalih poročil ter publikacij, ki so trenutno težko dosegljive. Vesoljska fiziologija se je razvila na osnovi poskusov v hipergravitaciji. Prvotni cilj centrifugalnih laboratorijev je bil preučevati meje gravitacijske tolerance. Namesto nadaljnjih ekstrapolacij iz podatkov, ki so izhajali iz poskusov v hipergravitaciji, sta med leti 1945 in 1947 Gauer in Haber izvedla ekstrapolacijo do breztežnosti in prišla do izjemno natančnih napovedi, kaj se lahko zgodi s človekovo fiziologijo, če se človek nahaja v breztežnostnem okolju. Članek z naslovom "Človek v breztežnostnih pogojih", ki je bil objavljen v nemškem vestniku German Aviation Medicine World War II Volume 1: 641–644, je bil prvi znanstveni članek, ki je postavil osnove za nadaljnji razvoj vesoljske medicine. Ta članek se lahko smatra kot začetek vesoljske fiziologije. Od takrat manipulacija s težnostjo predstavlja pravo orodje za fiziologe. Prispevek na kratko opisuje razvojne vidike v predvojnem obdobju v Berlinu in ZDA, prav tako omenja nekaj pionirjev na tem področju.

Ključne besede: *hipergravitacija, gravitacijska toleranca, laboratoriji z visokim težnostnim pospeškom, poročilo o delovanju*

INTRODUCTION

Pioneering work was needed in order to put man into space and bring him safely back to earth. When one reflects on this, mostly the rocket engineers and the first astronauts such as Russian Yuri Gagarin and American John Glenn, who were in orbit in 1961 and 1962 respectively who come to mind. The initial question was can man really survive in an environment where the forces of gravity were almost completely removed? One has to keep in mind that the forces of gravity have deeply shaped our bodies and minds and therefore its removal could have predictable, but also many unpredictable, and possibly life-threatening consequences. Since then, in the more than fifty years after the first manned spaceflights, it has been demonstrated on many occasions that man can survive for a considerable amount of time when put into space. A gravity-free environment is not, per se, a life-threatening factor.

The question still remains, what made pioneers in the fifties and sixties so confident that man could survive in space? Experimental proof could not be provided

because the force of gravity is omnipresent on earth and cannot be removed. However, O. H. Gauer and H. Haber (Gauer & Haber, 1950) elegantly circumvented this difficulty, what will be described later. In this short communication, we will confine ourselves mainly to the group around Gauer, because we believe that it is here that the most interesting developments occurred during the early years, keeping in mind, however that in many other places, particularly in the USA, similar work in the field of gravitational physiology was being done (Pace, 1977; Wood, 1987).

The centrifuge period (1935–1950)

Going back into the literature, one will find that many of the pioneers working in the field of gravitational physiology used centrifuges in order to explore the effects of gravity on the human body. When high-speed maneuverable airplanes came into use shortly before and during the Second World War, hypergravity was of interest for operational demands when using these high speed airplanes. Acceleration-induced loss of vision and consciousness demonstrated the urgent need to understand the causes of these blackouts which could lead to airplane crashes. For these purposes, huge human centrifuges needed to be constructed and put into operation which was done mostly in military institutions. Besides Berlin, such centrifuges were established at the Mayo Clinic in the United States under the guidance of Earl Wood (Wood, 1987) and at the Wright-Patterson Airfield in Dayton, Ohio, also in the United States, where Gauer worked between 1945 and 1951. Later, more of these centrifuges were installed in order to train pilots before flying high speed airplanes. Some of these centrifuge pioneers were working in the 1930s in Berlin. In the Aeromedical Research Center of the Air Ministry in Berlin, such a centrifuge was built and used by von Diringshofen, Strughold and Gauer (Kirsch and Winau, 1986). Another pioneer of aviation research who should also be mentioned was Nathan Zuntz who had previously worked in Berlin. When he rode in an airplane for the first time in 1912, he realized immediately that a new field of physiology had opened up. According to Zuntz, the otolith system should play a key role in this new field. Gunga described his scientific activities in 2009 in a book entitled "Nathan Zuntz, His Life and Work in the Fields of High Altitude Physiology and Aviation Medicine" (Gunga, 2009). The title of this book indicates that already in the first decades of the 20th century, Berlin was a leading center of what is now called Applied Physiology, which is more than just aviation medicine or space medicine. Gravitation physiology came on the academic scene at that time, and the result was a tremendous impact on the field of general physiology.

The most intensive scientific work on gravitational physiology was done from 1935 to 1945 by O. H. Gauer in Berlin. With the help of highly sophisticated technologies, he

succeeded in creating X-ray films of animals during different g-loads. A roentgen cinematographic recording technique allowed blood volume shifts along the body axis to be made visible step by step on a centrifuge during increasing g-loads. It became clear that blood volume shifts which led to a depletion of the intrathoracic blood volume stores of the body were the cause of blackouts during airplane manoeuvres. The heart was not filling at a sufficient rate for an adequate stroke volume and hence cardiac output. Generally, it was the aim of these centrifuge studies to explore the limits of g-tolerance by exposing the subjects to controlled increasing g-loads (Gauer, 1950; Wood, 1987).

All these activities in Berlin were halted after the war. The results of these activities, however, were well known to the Americans apparently from some publications written in German (Gauer, 1950; Kirsch & Winau, 1986). After the war, scientists who had worked in this field were gathered in Heidelberg by the Americans. Heidelberg was chosen as a viable location for scientific work because it had not been destroyed during the war; moreover, the Americans expressed a liking for the city. Certain undamaged buildings such as the Kaiser Wilhelm Institute for Medical Research were selected to host the scientists for the duration of their stay in Heidelberg. The first German scientist to arrive there was O. H. Gauer on the 20th of September, 1945. Here they could write down their results and if necessary, finish their experiments. The many results of these pioneering experiments were published after the Second World War in 1950 in the United States. Nowadays, only few copies of these papers are still available. The two volumes published in the United States were entitled "German Aviation Medicine World War II" (Gauer, 1950).

The Heidelberg period

In these two volumes, German scientists put together the data they had collected before and during the Second World War (Gauer, 1950). This was a part of Operation Paper Clip, during the exploitation of German science.

Food, housing and other materials were provided in Heidelberg by the Americans. Living in Germany at that time was extremely difficult and most of the scientists were happy to make a living for their families and themselves. We were able to interview some of the Germans and Americans who lived in Heidelberg at that time. Our work was supported by a grant from the Deutsche Forschungsgemeinschaft (Kirsch & Winau, 1986). The situation there was described by Col. Benford in a small booklet of which only a few copies still exist. The title of the book is Report from Heidelberg, written by Col. Benford. This small booklet gives an insight into the life at this centre immediately after the war. The purpose of this centre in Heidelberg was to support the exploitation of German science in the post-war period.

Special pieces of laboratory equipment were brought to Heidelberg, but most could not be put into action again. The scientists had time to write down and to discuss

their materials in detail. Over the course of this process, Gauer and Haber (Gauer & Haber, 1950) had the idea that instead of extrapolating forward to higher g-loads, it would be better to extrapolate downward to zero-g. When, for instance, under increasing g-loads the heart rate increased in proportion to the g-stress, this allowed an extrapolation of the limits of g-tolerance, among other things. In a similar way, the contour of the heart changed, indicating lower heart volumes under g-stress. These data were collected from animal experiments. The cardiovascular changes, especially heart function under g-stress, were described by Gauer in detail (Gauer, 1950). Also blood volume shifts along the body axis were mentioned. These parts of the report are still worth reading because they contain much information which can currently be obtained in a daily clinical routine, applying modern imaging techniques.

This work was far ahead of its time with regards to the modern cardiology and cardiovascular physiology of 1945–1947. The authors eventually arrived at the conclusion that direct disturbances of respiration and circulation in the absence of gravity are not to be anticipated. This kind of research could not have been done in a German university at that time due to the scarcity of funding available for scientists.

Surprisingly enough, Gauer and Haber foresaw problems in motor control because of the decreased input from the proprioceptive system and failure of the labyrinthine reflexes. They predicted kinetosis problems. All of these predictions came true. From this simple backward extrapolation from high g-loads towards zero g, many assumptions could be made (Gauer & Haber, 1950). Their predictions were far from mere speculation. This was for the first time that zero-g was no longer a matter of fantasy or guess-work.

Man under gravity-free conditions

In the first volume published in 1950, the results of these discussions were put together in an article entitled "Man Under Gravity-Free Conditions". The authors were O. Gauer and H. Haber (Gauer & Haber, 1950). Haber was an astrophysicist working in Berlin during the war. He joined the group around H. Strughold without previously having had contact with these scientists working in the field of human physiology. It was apparently Haber who calculated the energy requirements in order to escape from the gravitational field of the earth showing that this might indeed be possible (Gauer & Haber, 1950). Apparently the combination of a physiologist and an astrophysicist was necessary to create the new field of space physiology together under circumstances which could only have existed during the post-war period.

This article had far reaching consequences for the authors. The Americans thought that a connection existed during the war between the German rocket engineers and the

physiologists preparing manned space flight. This, however, had never been the case. Both groups were working independently of each other in Germany. Another consequence was that the Americans offered research positions to some of the scientists so that they could come to the United States. Among them was O. H. Gauer. Due to their publications coming out from the Aero Medical Laboratory Air Material Command, Wright-Patterson Air Force Base, Dayton, Ohio, the scientists became known to the American scientific community. Gauer moved from there to Duke University, North Carolina. Here he was back in an academic atmosphere where he felt he belonged to and which he had left since his early days in Heidelberg.

The academic period of gravitation physiology

The results extracted in the post-war period from the data were tremendous. They were published mostly in short abstracts between 1950 and 1956 (Gauer, Henry, Sieker & Wendt, 1951; Henry & Gauer, 1951). For details, one still has to look in the two previously mentioned volumes (Gauer, 1950).

In 1951, an abstract appeared in Federation Proceedings with the authors J. P. Henry and O. Gauer. Herein it was mentioned for the first time that a connection between blood volume and urine flow should exist. They suggested that changes in the size of the heart, in other words the distension of the heart, causes these changes in urine flow by activating stretch receptors located in the lungs and in the heart chambers, with arterial pressure remaining unchanged. A short time later, another short communication appeared in The American Journal of Physiology where heart and lungs were looked at as receptor regions controlling blood volume (Gauer, Henry, Sieker & Wendt, 1951). In addition, in this abstract for the first time the term "low pressure side" was used to describe what was earlier named "venous side of the circulation". What is currently described in textbooks as the Gauer-Henry reflex originates from these two abstracts. The terms high and low pressure side of the circulation to name the arterial and the venous side of the circulation apparently also stem from these authors. Both authors indicated during personal communications that the original idea for this concept of volume control of the circulation was derived from the centrifuge experiments.

In 1956, in Circulation Research, a series of four papers appeared which were based on human and animal experiments, therein the whole concept of blood volume control was laid out (Gauer, Henry & Sieker, 1956; Gauer, Henry, Sieker & Wendt, 1951). As the authors told it, it took several years till the manuscripts were accepted for publication. The ideas issued were too new in order to be accepted. A review article published in 1963 finally summarized the story of fluid volume control at that time (Gauer & Henry, 1963). Apparently, a quiet academic atmosphere was needed to harvest the fruits from this period.

If one looks back now on the developments of zero-g physiology, one can say that this field grew out of hypergravity physiology. Therefore, the subtitle of a paper by Nello Pace – "Weightlessness, a Matter of Gravity" – is fully correct and understandable (Pace, 1977). This field has enriched our knowledge in physiology. Much work was done outside of the universities. It is still the case, however, that our knowledge about the historical background of this field is rather incomplete and much more research needs to be done in this field.

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