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Professor Manuel Rodríguez Gómez and the tuberous sclerosis complex paradigm

Professor Manuel Rodríguez Gómez e o paradigma da Esclerose Tuberosa

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ABSTRACT

The authors present an historical review of aspects of the life of Professor Manuel R. Gómez, a Spanish neuropediatrician, who graduated in Havana and is known internationally for his work while he was in charge of Pediatric Neurology at the Mayo Clinic in Rochester, USA. His main contribution was related to the tuberous sclerosis complex, demystifying the Vogt triad previously used as a diagnostic criterion, and he was considered the "father of the tuberous sclerosis complex " in the USA.

Keywords: Tuberous sclerosis.

RESUMO

Os autores apresentam uma revisão histórica sobre aspectos da vida do professor Manuel R. Gómez, neuropediatra espanhol, formado em Havana e conhecido internacionalmente pelo seu trabalho à frente do serviço de Neurologia Pediátrica da clínica Mayo em Rochester, EUA. Sua principal contribuição esteve relacionada com o complexo esclerose tuberosa desmitificando a tríade de Vogt até então usada como critério diagnóstico da doença, pelo que foi considerado o 'pai do complexo esclerose tuberosa' nos EUA.

Palavras-chave: Esclerose tuberosa.

This year, Professor Manuel Rodríguez Gómez would have turned 90 years old. Considered the most well-known Spanish neuropediatrician[1], Professor Manolo Gómez, as he was called by his friends, developed a legion of admirers, for his simplicity, ease of communicating and transmission of knowledge, and dedication to his profession and his patients. He is the reason that the Tuberous Sclerosis Alliance recognized his trajectory by offering an annual award with his name. This award is given in memory of Manuel R. Gómez, MD, the "father of the tuberous sclerosis complex (TSC)" in the USA. Nominees are those who have made a significant impact on our understanding of TSC in research and/or impacted the delivery of clinical care for individuals with TSC[2]. Dr. Gómez provided care and compassion for hundreds of individuals with TSC during his career, and he sparked interest in the diagnosis and clinical care of individuals with TSC.

Manuel Rodríguez Gómez

Manuel Gómez was born on July 4, 1928 in Minaya, Albacete, Spain and, according to his friend and prominent neuropediatrician, Ignacio Pascual-Castroviejo, few have had such an intense life trajectory[1]. When Manuel was 12 years old, his father, who was a pharmacist and doctor, moved with his family to Havana, Cuba, where he spent his youth and studied medicine at the University of Havana, graduating in 1952. On the day of his graduation, in the heat of the party, he protested against the dictator Batista and, after spending a few hours under arrest, had to leave the island at night with only what he had on, headed for the United States. At that time, Manuel decided that his surname Rodríguez would be reduced to an initial, since he identified much more with his mother's surname of Gómez, which is the name he subsequently gave his children. He recovered 'Rodríguez' in his appearance as an author in the

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book *Neurocutaneous Diseases*, which he edited in 1987, and which remains the most complete treatise on neurocutaneous disorders. This was a tribute to his father, whom he met again during the Pan American Congress of Pediatrics in Havana in 1984, 32 years after last seeing him, as Manuel R. Gómez was mistakenly considered to be anti-Castro and was not allowed to enter Cuba. In May, 1997, he came to Curitiba, Brazil, having been invited to the International Symposium of Neurosciences (Figure).

Dr. Manuel R. Gómez is known primarily for his great professional career as head of the section of Pediatric Neurology of the Mayo Clinic of Rochester, Minnesota, USA, as well for his extensive scientific production. He was a founding member of the American Child Neurology Society, the International Child Neurology Association, and the Ibero-American Academy of Pediatric Neurology, as well as having received the first Ramón y Cajal Prize awarded by the latter, in Viña del Mar, Chile, in 1996. He had previously received the Hower Award from the American Child Neurology Society and the Leader Award from the National Tuberous Sclerosis Society. In addition, he was an Honorary Member of several scientific societies. He was also part of the editorial committees of most of the international magazines of Pediatric Neurology. He died on January 21, 2006, after a long illness (Parkinson's disease) and leaving his wife Joan, and their four children, Christopher, Gregory, Douglas and Timothy.

Tuberous sclerosis

The characterization of tuberous sclerosis has been a cumulative process, possibly owing to its multisystem manifestations[3]. Even though many of the signs and symptoms could be identified in isolated case reports, in 1835, the French dermatologist Pierre François Olive Rayer, when publishing his skin diseases atlas, described 'vascular vegetations', without associating it with a medical condition. Tuberous sclerosis complex was first described by von Recklinghausen on March 25, 1862, at the meeting of the Berlin Obstetrical Society. He presented a newborn baby who "died after a few breaths" because of multiple cardiac "myomata." The baby's brain contained numerous sclerotic areas, although von Recklinghausen did not elaborate. Although von Recklinghausen's patient almost certainly had TSC, his appreciation of its clinical manifestations was clearly rudimentary[4].

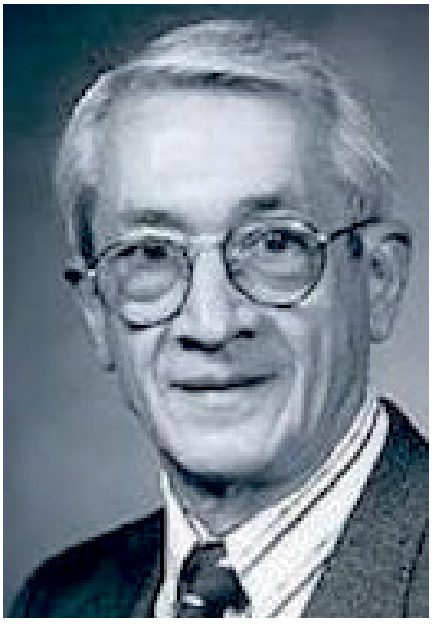

Figure. Prof. Manuel R. Gómez.

The first clear description is credited to Desire-Magloire Bourneville. In 1880, Bourneville treated a 15-year-old girl with a history of seizures, psychomotor retardation, and "confluent vesicular-papular eruption on the nose, cheeks, and forehead". Postmortem examination revealed hard, dense, tuber-like lesions in the cerebral gyri, which Bourneville named *sclérose tubéreuse des circonvolutions cérébrales*[4].

Nevertheless, Bourneville's understanding of TSC was initially limited. He noted his patient's facial angiofibromas but concluded that they were coincidental. Bourneville and Brissaud would later associate renal tumors with TSC.

The genetic nature of TSC was quickly recognized. In 1885, only five years after Bourneville's report, Balzer and Menetrier described TSC in a mother and daughter.

Tuberous sclerosis complex is a dominantly-inherited disorder of cellular differentiation and proliferation that invariably affects the brain, skin, kidneys, heart, eye, and other organs. The neurological manifestations of TSC include epilepsy, autism, cognitive and behavioral dysfunction, and giant cell tumors. Up to three quarters of the individuals with TSC have a spontaneous mutation. Two genes are responsible for tuberous sclerosis: TSC1 on chromosome 9q34 (which encodes the protein hamartin) and TSC2 on chromosome 16p13.3 (which encodes the protein tuberin)[5,6,7].

Neurological manifestations develop due to abnormalities in neuronal migration, cell differentiation and excessive proliferation and are expressed as epilepsy, school difficulty, intellectual deficiency and psychiatric disorders.

In 1908, Heinrich Vogt proposed quasi-diagnostic criteria for TSC, a triad consisting of epilepsy, "idiocy," and adenoma sebaceum (now called facial angiofibromas). Most individuals who manifest all three features of Vogt's triad will, in fact, have TSC, but a clinician using Vogt's triad would likely fail to diagnose half the TSC patients that are now recognized.

The German pediatric neurologist Heinrich Vogt established the diagnostic criteria for TSC, firmly associating the facial rash with the neurological consequences of the cortical tubers. Vogt's triad of epilepsy, mental retardation, and facial angiofibromas held for 60 years until research by Manuel Gómez discovered that fewer than a third of patients with TSC had all three symptoms[8].

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