Professor Peter Kubisz (1942–2022)—Un hommage à trois étincelles

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Semin Thromb Hemost 2023;49:209–211.

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Un hommage à trois étincelles, "*a tribute to three glints*" is the title which I have elected for this manuscript devoted to the recognition of an intimately intertwined triad: Professor Peter Kubisz, recently deceased, the 50th anniversary of *Seminars in Thrombosis and Hemostasis* (STH), and the 40th anniversary of the *Sticky Platelet Syndrome* (SPS).

La première...

Professor Peter Kubisz was born on June 13, 1942, in Třinec, Czechoslovakia. At age 12, he was gifted a microscope, a gift that defined his future. As a result of his interest in platelet function, he built and employed the first aggregometer in Czechoslovakia, while working with Professor Parizkom. In 1969, he completed his internship with Professor Jacques Caen in the Hôpital Lariboisière in Paris, France. Between 1970 and 1980, he was responsible for the Hematology Clinic at the University of Oran (Algiers). He later conducted and developed his research activities in Martin, and in the Jessenius Faculty of Medicine, in current day Slovakia. After the dissolution of Czechoslovakia in 1992, he became Chief of the Slovakian Health Ministry. He was very active in the *International Society of Hematology*, the *Danubian League against Thrombosis and Hemorrhagic Disorders*, and the *Slovakian Society of Hemostasis and Thrombosis*. Professor Kubisz was also the Chief Expert in transfusions at the Ministry of Health of the Slovak Republic, as well as Head of Hematology at the Ministry of Health of the Slovak Republic and a member of the advisory council of the Ministry of Health. For many years, he was also a member of the State Institute for Drug Control (ŠUKL), a member of the Categorization Commission of the Ministry of Health of the Slovak Republic, Vice Chairman of the Committee of the Society of Hematology and Transfusion (HaTS), Slovenská lekárska spoločnosť (SLS) or Slovakian Center for Diagnosis, and as of 2006, he became the President of the Slovak Society of Hemostasis and Thrombosis (SSHT) SLS. He was also involved in the study of angiogenesis in lower limb ischemia and the practice of autologous stem cell transplantation, having performed the first autograft in Slovakia in 2006. Professor Kubisz sadly passed away on September 9, 2022, at age 80. He was one of the more prolific investigators and writers on SPS and with his colleagues, he contributed three major publications to STH,[1–3] that defined seminal details on SPS:

1. Kubisz P, Stasko J, Holly P. Sticky platelet syndrome. Semin Thromb Hemost. 2013 Sep;39(6):674–83.
2. Kubisz P, Ruiz-Argüelles GJ, Stasko J, Holly P, Ruiz-Delgado GJ. Sticky platelet syndrome: history and future perspectives. Semin Thromb Hemost. 2014 Jul;40(5):526–34.
3. Kubisz P, Holly P, Stasko J. Sticky Platelet Syndrome: 35 Years of Growing Evidence. Semin Thromb Hemost. 2019 Feb;45(1):61–68.

La deuxième...

The journal STH was founded in 1974; accordingly, the 50th anniversary of its foundation will be celebrated in 2024. According to the *Journal Citation Reports*, its impact factor in 2021 was 6.398. Scientists in low- and middle-income countries (LMICs) face multiple quandaries when attempting to publish their work in journals published in high-income countries (HICs). This has led to what is now called "…… *the lost science of the third world: Many researchers in the developing world feel trapped in a vicious circle of neglect and - some say - prejudice by publishing barriers they claim good science to oblivion*."[4]

STH provides a forum in which scientific data originating in LMICs can be published in a journal originating in HICs. The editorial team have been supportive of physicians working in underprivileged circumstances and this positioning deserves recognition. The support that STH provided to enable the publications of Professor Kubisz, specifically in the area of SPS, which remains an area of debate, particularly for physicians working in HICs, is a clear example of the philosophy of STH and should be adopted by other journals.

article published online December 26, 2022

Issue Theme Celebrating 50 Years of Seminars in Thrombosis and Hemostasis—Part II; Guest Editor: Emmanuel J. Favaloro, PhD, FFSc (RCPA)

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0042-1760198.
ISSN 0094-6176.

By both promoting and supporting the publication of the salient features of SPS in STH, all based on the pool of knowledge that originated in a LMIC such as Mexico, STH has clearly demonstrated a role of inclusivity and now, 50 years after its initial publication, this journal has become one of the preferred worldwide channels to disseminate novel knowledge in the field of thrombosis and hemostasis.

La troisième…

Forty years ago, in 1983, the trio of Holiday, Mammen, and Gilroy coined, for the first time, the term "sticky platelet syndrome" (SPS) to describe a syndrome identified in a group of young persons with cerebral infarction and platelet hyperaggregability.[2] At the time, I had just returned to my hometown in Puebla, Mexico, after completing a postgraduate research fellowship in hematology at the Mayo Clinic in Rochester, MN, where I had the privilege of meeting other "giants" in the thrombosis and hemostasis field such as Walter Bowie, William Nichols, Kenneth Mann, and David Fass, among others. Although I did not directly work with them, our personal encounters resulted in my increasing interest in both thrombosis and hemostasis, since my focus had initially centered on hematological malignancies and bone marrow transplantation. Back in Mexico in 1999, I began initial studies on thrombophilia and two years later, in 2001, I became familiar with the SPS and decided to analyze its prevalence in Mexico. Our findings were published a year later, in 2002. I clearly remember the reaction of Prof. Rodger Bick, the then editor of *Clinical and Applied Thrombosis and Hemostasis*, when after reviewing our paper, stated that he was pleased to accept our "excellent paper" for publication in the journal. Never in my life had I received such a positive and encouraging comment on a potential publication. Professor Bick was a believer in the SPS and as a pupil of Professor Eberhard Mammen, he helped promote the term SPS. My own interest and research on the SPS persisted despite the contrary observations of many famous experts in coagulation, so-called "clotters," suggesting that the SPS was only a laboratory phenomenon or artifact and not a clinical entity per se. Our studies and those of other scientists working in this field were, have been, and are still criticized by several of these clotters who have neglected the need to investigate this condition in thrombophilic individuals, very frequently as a result of their inability or disinterest in searching for the condition's phenotype in their laboratories. In 2011, at a meeting organized by Ernesto Novoa in Montevideo, Uruguay, I met another believer in the SPS, Professor Peter Kubisz, and in 2013 I asked him to participate in a symposium on platelets in Cancún, Mexico; I was then able to include both endorsers and non-endorsers of the condition in a SPS symposium. In 2015, Professor Kubisz asked me to lecture on the SPS in Sarajevo, Bosnia-Herzegovina, during the Mediterranean League against Thrombosis meeting, where I had the chance to meet the Editor in Chief of STH, Prof. Emmanuel Favaloro. Subsequently, Prof. Kubisz invited me to lecture again on the topic in Martin, Slovakia in 2018, and I again crossed paths with Prof. Emmanuel Favaloro.

As a result of our interest in the SPS and with the assistance of various collaborators and of the previously mentioned giant clotters, we have now pieced several features of the SPS which can be summarized as follows[5–19]:

(1) The SPS is a phenotype of platelet hyperaggregability, defined by increased in vitro platelet aggregation after the addition of very low concentrations of adenosine diphosphate and/or epinephrine. The concentrations and dilutions of the agents are relatively well-standardized. An aggregometer is needed for the diagnosis of SPS, and its availability is one of the major obstacles to establish a diagnosis.
(2) The genotype is currently unknown, but several genes of platelet proteins are currently under study: platelet glycoprotein IIIa PLA1/A2; platelet glycoprotein VI, growth arrest-specific gene 6, coagulation factor V, integrin subunit beta-3, platelet endothelial aggregation receptor 1, serpin family C member 1, and serpin family E member 1, among others.
(3) The SPS phenotype is probably the expression of more than one genetic mutation that together, interact with other medical conditions or environmental factors such as diabetes mellitus, hormonal therapy, pregnancy, and others.
(4) The SPS may cause both arterial and venous thrombosis, the latter being more frequent.
(5) The SPS is a hereditary autosomal dominant trait.
(6) The SPS is the most frequent cause of hereditary thrombophilia in Mexico and perhaps, in other countries.
(7) Patients with SPS have been identified and treated in all continents of the world.
(8) The SPS is a frequent cause of miscarriages and obstetric complications (it would be good to know how many are associated with the antiphospholipid antibody syndrome).
(9) The SPS usually needs another thrombophilic condition to be fully expressed clinically as a thrombotic episode.
(10) The hyperaggregability in SPS reverts with antiplatelet drugs and the re-thrombosis rate in persons with the syndrome is very low when actively treated. Aspirin reverts the hyperaggregability state in most patients, but about one-quarter of cases warrant the administration of two antiplatelet drugs. It is therefore advisable to assess the SPS phenotype after initiating the antiplatelet drug, to define further treatment and its duration. Treating persons with SPS with oral anticoagulants does not reduce the re-thrombosis rate.
(11) Claiming that the SPS is a nonentity indicates that it is not being properly assessed or even considered, and may be detrimental to the patients; when diagnosed, it only requires a simple, inexpensive, and effective treatment that is tolerated by most patients: the use of low-dose aspirin and other antiplatelet drugs. But first, the diagnosis has to be considered and then established. There are many published descriptions of thromboembolic events in persons with SPS who are instructed to stop the

antiplatelet treatment and in which the authors still claim that "*the SPS is a myth*."

Coda

The objective of paying homage to the triad embodied by Professor Peter Kubisz, the 50th anniversary of STH, and the 40th anniversary of the SPS, all intimately connected, is to recognize the imbrication of science, human relations, and goodwill in the generation and dissemination of new knowledge, that in turn, may further benefit human health. Having been offered the opportunity to pay a tribute to this triad of "étincelles" has indeed, been a privilege.

Conflict of Interest
None declared.

References

1 Kubisz P, Stasko J, Holly P. Sticky platelet syndrome. Semin Thromb Hemost 2013;39(06):674–683
2 Kubisz P, Ruiz-Argüelles GJ, Stasko J, Holly P, Ruiz-Delgado GJ. Sticky platelet syndrome: history and future perspectives. Semin Thromb Hemost 2014;40(05):526–534
3 Kubisz P, Holly P, Stasko J. Sticky platelet syndrome: 35 years of growing evidence. Semin Thromb Hemost 2019;45(01):61–68
4 Gibbs WW. Lost science in the third world. Sci Am 1995; 273:92–99
5 Ruiz-Argüelles GJ, López-Martínez B, Cruz-Cruz D, Esparza-Silva L, Reyes-Aulis MB. Primary thrombophilia in Mexico III: a prospective study of the sticky platelet syndrome. Clin Appl Thromb Hemost 2002;8(03):273–277
6 Ruiz-Argüelles GJ, Ruiz-Delgado GJ, López-Martínez B. The sticky platelet syndrome: a frequent but unrecognized cause of thrombophilia [in Spanish]. Rev Invest Clin 2002;54(05):394–396
7 Ruiz-Argüelles GJ, López-Martínez B, Valdés-Tapia P, Gómez-Rangel JD, Reyes-Núñez V, Garcés-Eisele J. Primary thrombophilia in Mexico. V. A comprehensive prospective study indicates that most cases are multifactorial. Am J Hematol 2005;78(01):21–26
8 Ruiz-Argüelles GJ, González-Carrillo ML, Estrada-Gómez R, Valdés-Tapia P, Parra-Ortega I, Porras-Juárez A. Primary thrombophilia in México. VI: lack of statistical association among the inherited thrombophilic conditions [in Spanish]. Gac Med Mex 2007;143(04):317–322
9 Ruiz-Argüelles GJ, Alarcón-Urdaneta C, Calderón-García J, et al. Primary thrombophilia in México VIII: description of five kindreds of familial sticky platelet syndrome phenotype. Rev Hematol Mex 2011;12(02):73–78
10 Ruiz-Argüelles GJ, Garcés-Eisele J, Camacho-Alarcón C, et al. Primary thrombophilia in Mexico IX: the glycoprotein IIIa PLA1/A2 polymorphism is not associated with the sticky platelet syndrome phenotype. Clin Appl Thromb Hemost 2013;19(06): 689–692
11 Moncada B, Ruíz-Arguelles GJ, Castillo-Martínez C. The sticky platelet syndrome. Hematology 2013;18(04):230–232
12 Ruiz-Arguelles GJ. Comment on sticky platelet syndrome. Semin Thromb Hemost 2014;40(02):273
13 Velázquez-Sánchez-de-Cima S, Zamora-Ortiz G, Hernández-Reyes J, et al. Primary thrombophilia in México X: a prospective study of the treatment of the sticky platelet syndrome. Clin Appl Thromb Hemost 2015;21(01):91–95
14 Ruiz-Delgado GJ, Cantero-Fortiz Y, Mendez-Huerta MA, et al. Primary thrombophilia in Mexico XII: miscarriages are more frequent in people with sticky platelet syndrome. Turk J Haematol 2017;34(03):239–243
15 Azamar-Solis B, Cantero-Fortiz Y, Olivares-Gazca JC, et al. Primary thrombophilia in Mexico XIII: localization of the thrombotic events in Mexican mestizos with the sticky platelet syndrome. Clin Appl Thromb Hemost 2019;25:1076029619841700
16 Vallejo-Villalobos MF, Gomez-Cruz GB, Cantero-Fortiz Y, et al. Primary thrombophilia XIV: worldwide identification of sticky platelet syndrome. Semin Thromb Hemost 2019;45(04): 423–428
17 García-Navarrete YI, Vallejo-Villalobos MF, Olivares-Gazca JM, et al. Primary thrombophilia XV: antithrombotic treatment of sticky platelet syndrome worldwide. Ann Blood 2019; 4:15–15
18 Minutti-Zanella C, Villarreal-Martínez L, Ruiz-Argüelles GJ. Primary Thrombophilia XVII: A Narrative Review of Sticky Platelet Syndrome in México. J Clin Med 2022;11(14):4100
19 García-Villaseñor E, Bojalil-Álvarez L, Murrieta-Álvarez I, Cantero-Fortiz Y, Ruiz-Delgado GJ, Ruiz-Argüelles GJ. Primary thrombophilia XVI: a look at the genotype of the sticky platelet syndrome phenotype. Clin Appl Thromb Hemost 2021; 27:10760296211044212