



## *A walk to answer TTP together*

For several years now, Answering T.T.P. Foundation held an International TTP Day in September to raise awareness of this rare disease. Money is collected for research, but attention is also drawn to the stories of those affected or their family members, combined with training events and the provision of information material. The Answering T.T.P. Foundation was set up in 2009 by Sydney Kodatsky, who had TTP herself. (<https://www.answeringttp.org/patient-stories>).

We have already organized three TTP days in Switzerland: a hike on the Gurten, a walk along the renatured Aare between Bern and Belp, and a flea market stand in Bern.

Unfortunately, due to corona pandemic, we could not organize a patient event this year. During advent time, we would like to start shaping “TTP in Switzerland” publishing every day little stories until Christmas - hopefully we will also receive some reports from those affected. We will also continue this project next year as a monthly calendar.

On behalf of the Bern TTP team from research and clinic, I wish you a peaceful and informative advent season.

**Johanna Kremer Hovinga and her Bern TTP Team**





## 1924 – A new disease

### HYALINE THROMBOSIS OF THE TERMINAL ARTERIOLES AND CAPILLARIES: A HITHERTO UNDESCRIBED DISEASE

Eli Moschcowitz, M.D.

In the clinical pathological conference of January 10, 1924, Dr. Eli Moschcowitz, pathologist and internal consultant at Mount Sinai / Beth Israel Hospital in New York, presented the case of a deceased 16-year-old girl.

She became seriously ill after spending Labor Day in Rockaway Beach, Queens, New York, on the Atlantic Ocean. She was admitted to the Mount Sinai / Beth Israel Hospital with a high fever of up to 40 ° C, poor general condition and body aches. On physical examination, she was pale with some petechiae on the arms. The laboratory confirmed severe anemia (40g /L). The blood smear showed numerous normoblasts (red blood cells that left the bone marrow so early that they still have a nucleus. They are an expression of a massively increased production of red blood cells), but not sign of fragmentocytes, which are what we are mainly searching nowadays, and nothing was reported about the number of platelets. The urine test also showed a certain involvement of the kidneys. The blood cultures obtained remained negative, so the hypothesis of an infection was rejected.

The hospitalization was dramatic. After a few days, the patient complained of weakness in her left arm and leg, went into a coma and died a day later, a week after being admitted to the Mount Sinai / Beth Israel Hospital. During her hospitalization, the young patient was looked after or seen by various doctors, including by Dr. Emanuel Libman (who later gave his name to a disease, Libman-Sachs endocarditis), who was convinced that they were dealing with a new disease. **He was right!**

Dr. Moschcowitz, the pathologist in charge of the Mount Sinai / Beth Israel Hospital, performed the autopsy. In his report, he described for the first time thrombotic occlusions of arterioles and capillaries (small vessels) in the heart (where he found most of the thrombotic occlusions), in the spleen, in the kidneys and a few in the liver. These are what we consider now the classic findings of TTP.

Even though he had not examined the brain and given the clinical picture of the patient (probable stroke with weakness of the arm and leg on the left side and then a coma), the brain may have been affected too.

Moschcowitz suspected that the cause of death was a potent poison or toxin, which is both agglutinative and haemolytic, i.e. it had the ability to decompose red blood cells.

**Today we know the disease as Thrombotic Thrombocytopenic Purpura (TTP) or as it was first described as Moschcowitz syndrome.**



## 1924 – A new disease

### Referenzen:

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## Dr. Eli Moschcowitz

Eli Moschcowitz lived in New York for most of his life. He was born on August 2, 1879 in Girált in the Kingdom of Hungary, which was part of the Austrian and Hungarian Monarchy. He was the ninth and last child of Moritz and Rosa Moschcowitz-Friedländer after 5 girls and 3 boys, including their 14-year-old brother Alexis, who later became a respected surgeon at the Mount Sinai Hospital in New York. In 1881 the family emigrated from Hamburg to the USA, the crossing took place by ship. Moschcowitz studied medicine at Columbia University College of Physicians and Surgeons in New York. After graduating in 1900, he followed an obligatory practical semester at Mount Sinai Hospital and then in 1903/1904 he went to Berlin, where he trained as a pathologist with Prof. Ludwig Pick. Back in New York, he became a pathologist at Beth Israel Hospital and continued his education in clinical medicine. In 1920 he moved to Mount Sinai Hospital, which soon merged with Beth Israel Hospital and became one of its directors, as well as professor of clinical medicine at his alma mater at Columbia University in New York. He held both positions until he retired in 1945. During his career, he wrote more than 80 scientific papers, many with groundbreaking observations, such as the first description of TTP, changes in the blood count (eosinophilia) as a result of allergic reactions, on pulmonary hypertension or on the cause of arteriosclerosis. He was one of the first to see connections between the psyche and organic diseases (e.g. stress and high blood pressure or stomach ulcers, etc.). He was a valued internist, scholar, and scientist. His colleagues admired his diagnostic skills in solving unusual cases. He liked to travel - before the Second World War he was in Europe almost every year, as the numerous preserved ship passenger lists of the New York port authorities have shown. Later he went by steamship to South Africa, South America and Hawaii. He was a lover of music and art, books and good food, a long-time member of the Manhattan Chess Club, and apparently a magician. He was active well into old age, writing scientific articles and practicing until his death on February 23, 1964 at the age of 82.



**Dr. Eli Moschowitz**



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2. Baehr G. Foreword. Journal of the Mount Sinai Hospital 1945; XII (No 1, May-June)
3. Lilienthal H. Eli Moschowitz – on the doorstep of the hospital. Journal of the Mount Sinai Hospital 1945; XII (No 1, May-June):1-4



## The Mount Sinai Hospital in New York – for almost 100 years a TTP working place

The Mount Sinai / Beth Israel Hospital in New York plays an important role in the history of the TTP. Not only the world's first TTP patient was hospitalized, but also Dr. Eli Moschowitz's and Dr. HM. Tsai worked here. He described the Von Willebrand factor-splitting protease, the "scissors" or the Swiss Army Knife, at the same time as our team in Bern under the direction of Prof. Miha Furlan. But we come to Dr. HM. Tsai and to Prof. Furlan another day.

The Mount Sinai Hospital was founded in 1852 to provide medical care to the rapidly growing Jewish immigrant community in Manhattan. A suitable piece of land on New York's rural periphery was quickly located and acquired, just south of the Empire State Building built in the 1930s. At that time, sheep were still grazing here, as well as the residents of New York were picking tomatoes or roasting potatoes on campfires in this area. The foundation stone was laid on Thanksgiving in 1853 and the 45-bed hospital opened its doors to patients on June 5, 1855. In the first year, 216 patients were treated, but only 16 of them could pay for their treatment. The hospital was soon bursting at the seams and the need of a new building arised. As the population continued to grow rapidly, the Mount Sinai Hospital moved to a larger area on the east side of Central Park in East Harlem, Manhattan, where is still located today.

Since the establishment of the Mount Sinai / Beth Israel Hospital, many pioneers have worked in its premises. To name an example, prof. Abraham Jacobi as founder of paediatrics and later president of the American Medical Association, was so popular and respected that envious dodgy general practitioners and quacks employed a doppelgänger to lure patients into their clinics. Further examples are Prof. Jonas Salk, the inventor of the polio vaccination and the gastrointestinal specialist B.B. Crohn to name a few.



The Mount Sinai Hospital in New York – for almost 100 years a TTP working place



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1. Moschowitz E. Founding and Early Days of the Mount Sinai Hospital. *Am J Med* 1952;13(5):519-525
2. Baron JH. The Mount Sinai Hospital--a brief history. *Mt Sinai J Med*. 2000;67(1):3-5
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## Saint Nicholas around the world

At Murtenstrasse 40 (Bern, Switzerland), we, the TTP research group, share a big laboratory space with 9 other groups, and we consist of a total of 40 people coming from 13 different nations. We have different cultural traditions around Saint Nicholas and Christmas. Let's discover what our colleagues told us:

In Italy we don't have Saint Nicholas, but we have "la Befana". La Befana is a very friendly and amiable Italian witch who rides around on a broomstick. She brings candies and gift to the good children and coal to the bad children on the morning of Epiphany, January 6.

In Marocco we usually do not celebrate Christmas, but you can find Christmas trees and decorations around. We prefer to celebrate New Year's Eve.

In Belgium we celebrate Saint Claus and Saint Nicolaus. We have been told that he comes from Spain because he brings tangerines and nuts.

In Spain we mainly celebrate January,6, the three kings day.

In France we only celebrate Christmas.

In Lebanon it depends of the families. Some celebrates Santa Claus and Christmas, other not.

In India we do not celebrate Christmas because it is not part of our culture, but because we learned in school we celebrate anyway.

In China we don't celebrate Santa Claus, but me and my family live for so long in Switzerland that we celebrate it anyway with family and friends.

In Macedonia we do not celebrate Santa Claus, it is not fully part of our culture.

In Nepal we do not celebrate Christmas, it is not fully part of our culture.

In Germany, Switzerland and The Netherlands we celebrate Saint Nicholas. To discover more about this festivity, open the door tomorrow!







## Saint Nicholas

### Sinterklaas is the name of St. Nicholas in the Netherlands.



On the Saturday after Martini, in the middle of November, Sinterklaas arrives with his assistants in the Netherlands. They are warmly welcomed by many people, young and old, old and young. He brings tangerines, oranges, pepper nuts and other delicacies from Spain.

While Sinterklaas wears a white beard, a red cape, a bishop's mitre and a crook, his assistants (Zwarte Piet = Schwarz Peter) are dressed in splendid, oriental robes and their faces blackened with shoe polish. The latter has given rise to heated debates on racism in recent years, and there have even been calls for Sinterklaas to be abolished. Since then, in addition to the typical Zwarte Piet, you can also see helpers with green, blue or red make-up.

On his white horse, Sinterklaas rides across the land and the roofs, and comes into the houses through the chimney with his assistants. The children put their shoes or winter boots with an apple or a carrot for the horse, or a drawing or something handcraft for Sinterklaas in front of the fireplace or the front door. If Sinterklaas and Zwarte Piet are in the area, the children gifts are replaced by small gifts or treats, otherwise you may try again in the next evening. The actual festival is celebrated on the evening of December 5th. It's Pakjesavond (gift evening). On this evening Sinterklaas brings gifts, toys for children. The recipient usually gets the first letter of his name made of chocolate. Adults often have to guess the content of their gifts, funny rhymes or short poems serve as a hint.

### Samichlaus in Switzerland



Santa is living in a dark forest where he documents the good and bad behavior of all the children. He writes everything down in his book.

Once a year on December 6<sup>th</sup>, Santa travels with his donkey and Schmutzli to the children's homes. While Santa is dressed in a nice red robe, Schmutzli is clothed in brown rags, his face blackened by grime.

The donkey is carrying the heavy bag with all the gifts for the well behaved children, while Schmutzli carries the rod for the bad behaving children.

The children will tell Santa rhymes or poems and as a reward will get nuts, tangerines, gingerbread and chocolate from Santa.

Schmutzli will stuff the bad behaving children into the now empty bag, carrying them back to the forest where they become Santa's helper for one year.



## Saint Nicholas

### Saint Nicholas in Germany



St. Nicholas Day or Nikolaus sometimes also spelled Nikolas is the Patron Saint of Children and on December 6th children throughout Germany wake up to find small gifts and goodies in their shoes.

On the evening of December 5th, children not only place a boot or shoes outside their bedroom doors, but they also have to clean them first, hoping that St. Nicholas will fill them with presents overnight.

The German Nikolaus tradition is still very strong in Germany and to this day children look forward to cleaning their shoes and receiving small gifts.



## Thrombotic thrombocytopenic Purpura – a concept was born

Already long before the platelets (thrombocytes) were identified as component of the blood, the German doctor and poet Paul Gottlieb Werholf, described in detail the first case of thrombocytopenia purpura. He was really famous in Hannover as it was the royal physician.

He called this clinical picture *morbus maculocosis hemorrhagica*, because the patient presented petechiae (the purpura) and a bleeding tendency in particular in the area around the mucosae.

The rise of high microscopy resolution in the middle of 19th century helped in finding the connection between the discovery of platelets and so called Werholf syndrome. Today we know this disease as idiopathic thrombocytopenic purpura (ITP), causing 50-100 cases per million per year. ITP occurs 50 times more frequently than TTP. It comes often after infections and it affects children more than adults. In many cases, thrombocytopenic purpura has presented a benign course. In children it resolves spontaneously, as it is not happening for TTP.

In 1947 the physician Karl Singer treated in Chicago a 11-years old girl with thrombocytopenic purpura, she died after a week of hospitalization. She had a similar disease course as the girl treated some years before by Dr. Eli Moschocowitz (Story Advent calendar Day 1). In his report, Singer stressed the difference of his case to the well known and more frequent ITP. He described all the histopathological findings he could observe. He also reported together with this case 11 other additional cases including Dr. Eli Moschocowitz's case and linked together the clinical findings with laboratory results. This new disease was, indeed, quite rare, but highlighted the continuous occurrence of certain distinct signs present in all 12 cases.

Singer recognized that the thrombocytopenic purpura was caused by platelet consumption in small vessels. He was the first one calling this new disease thrombotic thrombocytopenic purpura, to mark the clear difference with ITP. The name remained.

### Sources:

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## The other side of TTP: our research team

Today, we look at TTP in Switzerland, from the research team prospective. Isabella, our fantastic lab-technician and coordinator of the Hereditary TTP Registry, told us about her research:

“I’m working for the TTP Registry since January 2015 as a coordinator and also supporting Erika Tarasco our Registry manager.

From the beginning on, when I was getting to know all the theory about TTP, I realized how strongly patients are suffering when diagnosed with TTP. We also enroll family members and therefore whole families are affected by one patient’s diagnosis.

I am also working in the lab doing research. This is also a good way to find out more about TTP and hopefully to contribute to a relief or even cure. It motivates me to go on and I’m still excited to learn more about TTP every day”.

