One hundred years of *Haematologica*

Paolo Mazzarello

Department of Brain and Behavioral Sciences and University Museum System, University of Pavia, Italy

E-mail: PAOLO MAZZARELLO - paolo.mazzarello@unipv.it

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The historical-scientific background

Hematology as a separate specialty, with its own methodology and hospital wards, only began to emerge between the nineteenth and the twentieth centuries. Before then, the pathophysiology and the clinical practice of hematologic diseases were mainly considered to be simply a part of internal medicine. However, the use of the term 'hematology' was, in fact, much older. In 1743, Thomas Schwencke (1694-1767), professor at the Faculty of Medicine of the University of The Hague, and also a physician to Wolfgang Amadeus Mozart during his concert tour in the Netherlands in 1765, published a volume entitled *Haematologia, sive sanguinis historia*. A book written by Martin Schurig (1656-1733), a doctor from Dresden, was published in 1744 which bore the term 'hematology' in the title: *Haematologia historico-medica, hoc est sanguinis consideratio physico-medico-curiosa etc.*

The turning point that brought hematology into the modern age was the introduction of cell theory in the mid-nineteenth century, according to which all body organs and parts of living beings, including the blood, were composed of many elementary 'bricks', the cells, and by what they produced through their different functions.[1] Although this represents the theoretical prerequisite for the development of this field of medicine, along with biology, its real foundations could only be laid, on the one hand, by the development of modern microscopy (and related cytological staining techniques) and, on the other, by the development of chemical methods to study the blood. The invention of the achromatic microscope by Giovanni Battista Amici (1786-1863) in 1824 and the development of staining procedure in histology based on aniline dyes by Paul Ehrlich (1854-1915) were particularly important.

The second half of the nineteenth century was certainly a crucial period for the investigation of blood components. Although the erythrocytes had been observed by the Italian Marcello Malpighi (1628-1694) in 1665, and clearly described by the Dutch Antoni van Leeuwenhoek (1632-1723) in 1674,[2] they became a subject of functional study in relation to pathological conditions only in the second half of the nineteenth century. An important scientific step in the history of hematology was the discovery of the hematopoietic function of bone marrow by Ernst Neumann (1834-1918) and Giulio Bizzozero (1846-1901) in 1868.[3] Another important development in this field of medicine was the description by Paul Ehrlich (who used the aniline staining technique in his degree thesis) of various types of leukocytes on the basis of their affinity for specific dyes. Although there had been some earlier vague descriptions of platelets, they were clearly observed almost simultaneously by various authors from 1878 to 1882, in particular by Georges Hayem (1841-1933), Ernst Neumann and Giulio Bizzozero. Only the latter, however, was able to consider them as distinct elements unrelated to erythrocytes and leukocytes, and to clarify their fundamental role in the formation of the white thrombus capable of blocking hemorrhage. Moreover, as early as 1869, Bizzozero in Pavia had described the megakaryocytes as "giant cells".[4] However, it was not until 1906 that James Homer Wright (1869-1928) hypothesized that platelets derive from bone marrow megakaryocytes.[5]

Thus, it was during the second half of the nineteenth century that the fundamental cognitive elements from which hematology could develop as an autonomous discipline were laid down. The subsequent explosion of clinical and pathophysiological studies of blood disorders led to the need for specific publishing tools aimed at disseminating the results of the research. And so the first specialized journals for hematologic studies in normal and pathological conditions were founded. One of these that quickly became a focus of attention was *Folia haematologica* founded by Artur Pappenheim (1870-1916), one of the leaders of the emerging field of blood studies in physiology and pathology. Working on the development of erythrocytes in Rudolf Virchow's (1821-1902) Pathological Institute in Berlin, he became the

Figure 1. Guido Bizzozero.

pioneer of the line of inquiry that saw the origin of the erythroid and lymphoid lineages in a common ancestral element: a stem cell (Stammzelle). This was the "unicist" theory of the origin of blood cells, and the journal that Pappenheim had founded became an important means to spread his ideas.

The first two architects of *Haematologica*

An Italian physician, Adolfo Ferrata (1880-1946), joined Artur Pappenheim in 1909 to carry forward his specialization studies in hematology. Ferrata was born in Brescia and studied medicine at the University of Parma. He had very early on shown a marked aptitude for investigating new fields of medical-biological sciences.[6-8] By the time he graduated in 1904, he had already acquired a remarkable mastery of laboratory methods. This was further refined during a first period of study in Germany, in 1907, at the Institute of Pathology under the direction of Julius Morgenroth (1871-1924) who, with his teacher Paul Ehrlich, had introduced the concept of "complement" to indicate that fraction of the blood that favors the immune response. Shortly after his arrival, Adolfo Ferrata was able to demonstrate, through dialysis, the existence of two fractions of the complement (one soluble and the other part of the seroglobulins) that were inactive if taken individually but which reactivated if joined together. Ferrata spent 1908 in Italy but then returned to Germany, this time to the Pappenheim laboratory where he worked on the genesis of the morphological elements of the blood. The result of one year of hard work and intense study was a 130-page monograph, illustrated with four splendid color plates, published in collaboration with his German mentor on *Folia haematologica*. Pappenheim and Ferrata provided persuasive morphological evidence to show that the elements of blood had a unitary origin. This fundamental study began to impose a taxonomic order in a field of study that had become increasingly complex.

Figure 2. Adolfo Ferrata.

In 1912, back in Italy, Ferrata published *Morfologia del sangue normale e patologico*,[9] a book that can be considered to represent the birth of Italian hematology. In Italy, Ferrata very soon became the leader in his field. At the same time, he started his university career, although this was interrupted during the First World War when he became the Director of a military hospital in Brescia. By the beginning of the 1920s, Ferrata was working in Naples at the II Medical Clinic of the University, and very quickly showed he was ready to take a university chair. After other temporary positions, he taught at the University of Pavia between 1924 and 1925, and, he became full professor there in 1926. It was a position he was to hold until his death.

By this time, it had been clearly recognized that what was needed was an Italian journal dedicated to hematology. To help in this, Ferrata found another young scientist who, like him, had spent some of his most important formative years training in Germany: Carlo Moreschi (1876-1921).[10] Born in Cermenate, near Como, Moreschi had studied medicine at the University of Pavia as a member of the Borromeo College. During that time, he regularly attended the General Pathology Laboratory directed by Camillo Golgi (1843-1926). Moreschi quickly adopted the rigorous experimental approach promoted by Golgi and this is clearly evident in his first works, published in 1900, the year he graduated. Moreschi worked as an assistant to the Chair of Medical Pathology in Pavia, but in 1904 began a long scientific collaboration with the prestigious Institute of Hygiene of Königsberg, which continued until 1907. Partnerships with the bacteriologist Richard Pfeiffer (1858-1945), who had isolated *Haemophilus influenzae* in 1892, and the immunologist-hygienist Ernst Friedberger (1875-1932) were both extremely productive. After a brief period of work in Italy in 1907, he returned to Germany and worked in Frankfurt in the laboratory of Paul Ehrlich who, a year later, would receive the Nobel Prize for Medicine. Meanwhile, in 1907 and in 1908, Moreschi published the report of his important scientific discovery, the antiglobulin test. This was rediscovered by Robert (known as Robin) Coombs (1921-2006), Arthur Mourant (1904-1994), and Robert Russell Rice (1907-1984) in 1945. It is now generally referred to as the Coombs test (or the Moreschi-Coombs test). In 1998, recalling this research, Coombs wrote that, when the substantial paper about the rediscovery was ready, "Arthur Mourant, a considerable linguist, came across a paper in the German literature from 1908 by a certain Carlo Moreschi which described enhancement of red cell agglutination with an 'antiserum to serum'. An acknowledgement was added to the proofs as an addendum".[11-13] Back in Italy, Moreschi obtained a position as assistant professor at the University of Pavia, then, as we said before, he worked as a military doctor during the First World War. At the same time, his university career was also progressing. In 1916, he obtained a position as Associate Professor ("Professore Incaricato") of Clinical

Figure 3. Carlo Moreschi.

and Medical Pathology at the University of Sassari, Sardinia, and later the chair of the Medical Clinic in Messina, Sicily.

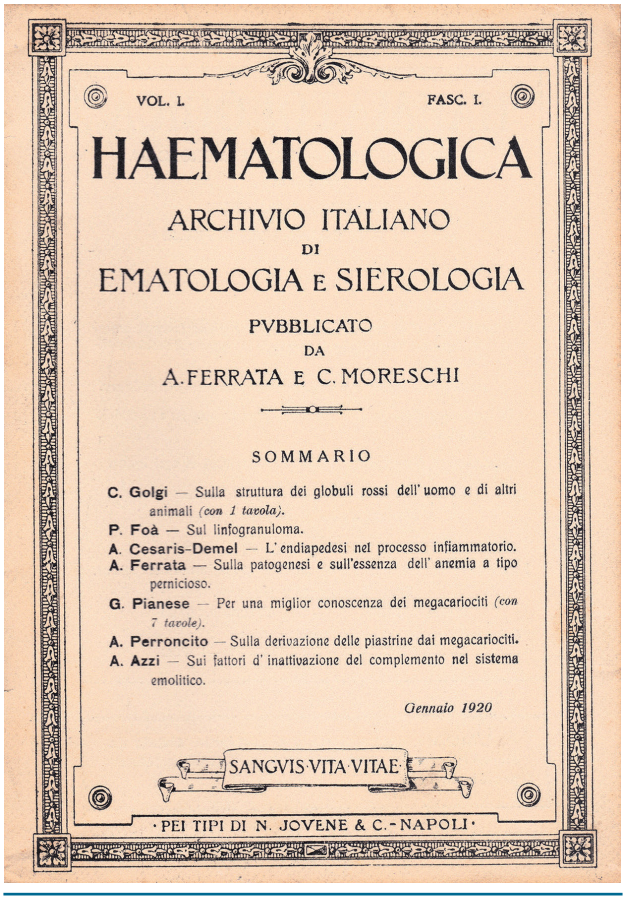
In 1921, while in Pavia, Moreschi showed the very serious symptoms of hemorrhagic smallpox, probably contracted in Messina while he was visiting a patient, and died on May 24th.

The year before, Ferrata and Moreschi had met in the historic Neapolitan café, the "Gambrinus", and during their discussion, *Haematologica* was founded. It was initially printed in Naples by the publisher "N. Jovene & Co." and then, from 1924, it was edited in Pavia.[14] The two founders became editorial managers of the journal, and from 1922, after the death of Moreschi, Ferrata continued in this role alone. It is evident how the model that inspired them was the journal founded by Pappenheim, *Folia haematologica*.

Haematologica: the beginning of a long story

Haematologica was founded in January 1920 under the best auspices. In fact, the first article had as its author the greatest living revolutionary of Italian medicine and biology, Camillo Golgi, Nobel prize winner in 1906 for his investigation of the structure of the central nervous system. During his life-time, Golgi made an enormous contribution to hematology and clinical pathology. In 1885-1892, he had described with great precision the various stages of development of the malarial parasites in the blood (which became known as the Golgi cycle), identifying the correspondence between the moment of their reproduction with the periodic febrile bouts (Golgi law).[15] So, the first series of articles in *Haematologica* were published under the most authoritative and prestigious name of Italian medicine, and the man who had taught Moreschi. It was a way to guarantee and certify the scientific credibility of the periodical, but also a sign of respect for the old pathologist. Golgi's article was based on a new gold chloride staining method and described the appearance of a central body resembling a kind of nucleus.[16] He immediately distanced himself from those researchers who supported the thesis of a persistence of a real, functionally active nucleus in red blood cells. Among these was Angelo Petrone, who had been defending this concept since 1897 on the basis of experiments conducted using his own particular method. However, Petrone's conclusion had been refuted by work carried out in Golgi's laboratory by Adelchi Negri (1876-1912) in 1899.[15] Petrone subsequently presented new observations that apparently seemed to confirm his old theory. The hypothesis of the existence of a nucleus in the red blood cells of mammals was, therefore, once again of some interest in Italian scientific circles. But Golgi pointed out that his investigations did not support this hypothesis, although he did not provide any alternative functional interpretation of his observation. These findings were subsequently interpreted as artifacts due to the technique used rather than to morphological peculiarities that actually existed in the cell cytoplasm.[17,18] In the same article, Golgi described the presence of the centrosome in white blood cells, while in a subsequent note he addressed the problem of the possible existence of the centrosome in erythrocytes.[19]

Immediately after the authoritative opening of the old master, whose studies were continued by his pupil Costanza Boccadoro (1893-1983),[20,21] the first issue of *Haematologica* contained contributions by some of the exponents of Italian medicine and, in particular, hematology. The pathologist Pio Foà (1848-1923) investigated the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HAEMATOLOGICA

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DA
A. FERRATA E C. MORESCHI

SOMMARIO

C. Golgi — Sulla struttura dei globuli rossi dell'uomo e di altri animali *(con 1 tavola)*.
P. Foà — Sul linfogranuloma.
A. Cesaris-Demel — L'endiapedesi nel processo infiammatorio.
A. Ferrata — Sulla patogenesi e sull'essenza dell'anemia a tipo pernicioso.
G. Pianese — Per una miglior conoscenza dei megacariociti *(con 7 tavole)*.
A. Perroncito — Sulla derivazione delle piastrine dai megacariociti.
A. Azzi — Sui fattori d'inattivazione del complemento nel sistema emolitico.

Gennaio 1920

SANGVIS VITA VITAE

PEI TIPI DI N. JOVENE & C. - NAPOLI

Figure 4. First issue of Haematologica.

Figure 5. Camillo Golgi.

nosographic problem of lymphogranuloma and its differentiation from tuberculous granuloma,[22] and another pathologist, Antonio Cesaris-Demel (1866-1938), published a paper on the stages of the diapedesis process.[23] There was also a very important paper by Ferrata on the pathogenesis of pernicious anemia.[24] Ferrata reported the complete disappearance of the megaloblastic erythropoiesis of the embryonic period as soon as the hematopoietic function of the liver begins. Ferrata's paper was a preliminary work which hinted at the therapeutic turning point that occurred a few years later with the introduction of hepatic treatment of pernicious anemia, which results in the rapid disappearance of megaloblastic erythropoiesis; as in the normal embryo, the liver's initial embryonic function makes the megaloblasts disappear. A few years later, Ferrata reviewed this treatment in the light of his 1920 observation in *Haematologica*.* Ferrata probably also made some attempts to treat patients with animal liver, but unfortunately he used cooked tissue, and did not observe any tangible effect.[25] The problem of treating pernicious anemia was taken up in a new way in subsequent works. Enrico Greppi (1896-1969) of the Medical Clinic of the University of Milan reported the case of a young man suffering from pernicious anemia and dyspeptic disorders of a probably infectious nature who was completely cured by transfusion.[26] Another remarkable work on the subject, published in *Haematologica* in German, came from Zoltan Alexander Leitner (1899-1981)[27] of the "Charité" Hospital in Berlin. He discussed the studies of George Richards Minot (1885-1950), George Hoyt Whipple (1878-1976), and William Parry Murphy (1892-1987) on the treatment of pernicious anemia with uncooked liver and with intramuscular liver extracts, which would earn them the Nobel Prize for Medicine in 1934.[28] Leitner suggested that extremely debilitated patients who required urgent intervention, or those in whom the gastro-enteric tract was seriously compromised, thus preventing adequate digestion, needed to receive a blood transfusion.

One of the most hotly debated hematologic arguments at the beginning of the 1920s was the origin of platelets from megakaryocytes. As many as 5 of the 31 articles published in the first volume of *Haematologica* dealt with the genesis of these corpuscles. In Ferrata's 1918 book *Le Emopatie*[29] (The Hemopathies), specific chapters were devoted to the various hypotheses:

– "Are platelets living and independent cells?"
– "Are platelets elements of variable and multiple origin, from erythrocytes, leukocytes and possibly from the vasal endothelium?"

*Carlo Bernasconi, personal communication. Carlo Bernasconi (1929-2014), formerly Professor of Hematology at the University of Pavia.

– "Are platelets derived from leukocytes?"
– "Are platelets derived from erythrocytes?"
– "Are platelets derived from megakaryocytes?"

Although Ferrata openly inclined towards the hypothesis that platelets are the third cellular element of blood and are produced by megakaryocytes, the topic remains a subject of discussion. Some articles published in *Haematologica* in 1920 were particularly relevant. The first written by Giuseppe Pianese (1864-1933) who worked at the Institute of Pathological Anatomy and Histology of Naples, concluded that platelets were not stable elements of blood and did not derive from megakaryocytes, but were formed in particular conditions, just as fibrin is formed from fibrinogen.[30] Golgi's pupil, Aldo Perroncito (1882-1929), who taught General Pathology at the University of Cagliari, Sardinia, had his doubts as to whether platelets where derived from megakaryocytes.[31-34] In fact, he suggested that the morphological evidence that supported this hypothesis was the consequence of experimental artifacts, since the medullary megakaryocytes ingested the platelets. So, since the megakaryocytes contained these corpuscles in their cytoplasm, it seemed that they produced them. In addition, platelets adhere to megakaryocytes and therefore the latter may seem to release them. The origin of the platelets was, therefore, according to Perroncito, still unknown. A precise and determined position in favor of the theory of the origin of platelets from megakaryocytes was taken by Giovanni Di Guglielmo (1886-1961) from Naples in a work performed under the direction of Ferrata.[35] Di Guglielmo observed how megakaryocytes could be present in the blood in some pathological conditions (chronic granulocytic leukemia) and were able to form platelets. He made a very accurate morphological description of this process, demonstrating that Perroncito's critical observations were wrong. In some beautiful color illustrations he showed the formation and release of platelets from megakaryocytes both through the fragmentation of their cytoplasm and *via* the emission of long cytoplasmic extroflexions.

In the years immediately following its foundation, *Haematologica* published numerous other works on the genesis of platelets.[36-41] Their derivation from megakaryocytes received increasing accreditation, although there was still room for alternative hypotheses. In the end, it was again Di Guglielmo who wrote the most lucid work on the origin of these corpuscles, reaffirming the correct thesis of their derivation from megakaryocytes.[42] He also confirmed his previous observations that these cells can enter peripheral blood in pathological conditions. The theory that megakaryocytes are present in the circulatory system (not only in pathological conditions but also in healthy subjects) and contribute to the formation of platelets has been definitively confirmed very recently with the documentation, in the mouse, of the release of platelets by the megakaryocytes migrated through the circulatory stream in the lung.[43]

From the start, serology and serodiagnosis of infectious diseases have always found a place in *Haematologica*.[44-50] But topics of a more hematologic nature continued to be at the center of the interests of the researchers who contributed to the journal. Following the cytological study of Golgi, some works published in the journal dealt with speculative (and sometime bizarre) hypotheses about the structure and shape of red blood cells.[51-54] Other investigations sparked a controversy over the priority of identifying the granule-filamentous substance in erythrocytes.[55] *Haematologica* has always published studies aimed at the chemical-physical characteristics of blood and hemoglobin.[56] One of the most important was a long article written by the physiologist Mario Camis (1878-1946) dedicated to the aggregating properties of hemoglobin that were rigorously studied under different conditions;[57] he also published a paper on the ultramicroscopic aspect of pure colloidal hemoglobin solutions studied, once again, under different conditions by means of the Zeiss microscope model which had been developed by Richard Adolf Zsigmondy (1865-1929) and Henry Siedentopf (1872-1940).[58]

However, the nature of megakaryocytes and their role in the production of platelets continued to be at the center of interest. The particular "budding" shape of the nucleus of megakaryocytes had opened up a specific question. Some cytologists/hematologists, like Ferrata and Pappenheim, believed that this aspect was the consequence of nuclear divisions not followed by cell separation. Other authors thought that megakaryocytes derived from the fusion of several cells. This was one of the most important topics of study at the Medical Clinic of Pavia. In the mid-20s, immediately following the arrival of

Figure 6. Giovanni di Guglielmo.

Ferrata as director and of his assistant Di Guglielmo, the Clinic had immediately become the most important center of hematology in the whole of Italy. The liberal environment assured by Ferrata's honest scientific attitude promoted the cultivation of very different ideas (although these were not always shared by the boss!). Thus, Di Guglielmo was able to argue that megakaryocytes derived from a process of cell fusion that eventually gave rise to their multi-nuclear appearance;[59] an idea shared by others.[60] There were also those who, playing devil's advocate, proposed the hypothesis of the dual origin of megakaryocytes, both by fusion and by nuclear "budding".[61,62]

From its first volume, *Haematologica* continued to publish many works dedicated to the clinical practice and clinical pathology of hematologic diseases. Of course, the founder of the journal, Ferrata, contributed works that resulted from his collaboration with members of the scientific school that was being formed around him (first in Naples, and then in Siena and Pavia), in particular with his most brilliant pupil at that time, Di Guglielmo. In addition to articles on pernicious anemia, studies appeared on the histogenesis of granulocytic leukemia.[63,64] on cytological changes in the malarial spleen,[65] and on histiocytic syndromes.[66] Di Guglielmo wrote an important work on erythremia for *Haematologica*, a field of study he personally introduced.[67] The paper described in depth two cases of acute erythremia (Di Guglielmo's disease) that had already been presented to the Medical-Surgical Society of Pavia in 1926, variously studied from different clinical, hematologic, and anatomical-pathological points of view. Many other areas of clinical hematology and related fields of study were also touched on, including: paroxysmal hemoglobinuria, the clinical and biological significance of Bence-Jones proteinuria, the pathogenesis of Gaucher disease, studies on leukemia, investigation of the forensic applications of hematology, and so on.

Haematologica has also always provided a means of making research performed outside Italy available to a wider readership, with works published in French, German and English. Thanks to the credibility and high professional profile of the director, Ferrata, the prestige of the journal immediately attracted the publication of studies produced by illustrious European names in the medical sciences. In 1924, Otto Lubarsch (1860-1933), director of the Institute of Pathology of the University of Berlin (known for defining carcinoid tumors) published a paper on the pathogenesis of thrombosis and embolism.[68] Shortly afterwards, the well-known pathologist Felix Marchand (1846-1928), who worked in Leipzig, published an article on the histology of the omentum.[69] An important paper was published in 1922 by Hal Downey (1877-1959) of the Department of Animal Biology of the University of Minnesota, in the US, a researcher who would become known the following year for the description of reactive lymphocytes (also known as "Downey cells"). The paper dealt with the structure and origin of lymph sinuses of mammalian lymph nodes.[70] In its first ten years, other studies were sent for publication in *Haematologica* from France,[71] Hungary,[72] Switzerland,[73,74] Austria,[75] Romania,[76,77] Belgium,[78] Russia,[79] Czechoslovakia,[80] and Brazil.[81]

Ups and downs

In ten years, Ferrata's management of *Haematologica* had allowed it to gain a position of great international prestige in the study of the physiology and pathology of the blood. Between the end of the 1920s and the beginning of the following decade, Ferrata's pupils from Pavia began to publish regularly in the journal. Many were destined to have important careers in Italian Hematology and Medical Clinic departments. Aminta Fieschi (1904-1991) was an active contributor to both clinical research and in cytological studies. Besides working at the Medical Clinic of Pavia, he also worked at the hospital in Cremona and, from 1930, at the Pavia Institute of Anatomy and Comparative Physiology.[82-87] Another important pupil of Ferrata was Paolo Introzzi (1898-1990), who worked for a time in Berlin with Zoltan Alexander Leitner and started to publish in *Haematologica* in the mid-'20s.** In one article, he proposed spleen puncture as a diagnostic procedure for pernicious anemia instead of bone marrow biopsy, a method that he proposed also applied to malignant granuloma.[88,89] The spleen remained his particular focus of interest and with Ferrata he proposed splenectomy to treat a case of primitive follicle-hyperplastic splenomegaly; the patient recovered.[90] In *Haematologica* he published studies in collaboration with Caterina Dessylla[91] of the Pediatric Clinic of Bologna and, above all, with Jörgen Nilsen Schaumann (1879-1953) of the Finsen-Institutet of Stockholm (who would give his name to Besnier-Boeck-Schaumann disease), with whom he studied the alterations of hematopoietic organs in acute lupus erythematosus.[92]

In 1931, Edoardo Storti (1909-2006) made his debut for *Haematologica* with a work on experimental anemia during an infection with *Botriocephalus*.[93] At the time he was a student of the Ghislieri College at the University of Pavia and attended the Institute of Anatomy and Comparative Physiology to prepare his degree thesis. A few years later he would become one of the main collaborators of Ferrata[94-96] and his last scientific heir.[97] At the same Institute of Anatomy and Comparative Physiology, his fellow student at the Ghislieri College, Vittorio Erspamer (1909-1999), also took his first steps in scientific research. In 1934, *Haematologica* published his study on schistosomiasis anemia in Libyan patients who he had examined during a scientific expedition.[98] Three years later he discovered serotonin in the intestines of experimental animals.[99,100]

Important works were published in the journal by the principal Italian hematologists of the day. Among them was Ferdinando Micheli (1872-1937), director of the Medical Clinic of the University of Turin, whose contribution was a paper on hemolytic anemia with hemoglobinuria and hemosiderinuria[101] (at the time called Marchiafava disease, but later to be known as Marchiafava-Micheli disease) and Giovanni De Toni (1895-1973), from the Pediatric Clinic of Bologna (whose

***Leitner was a friend of Ferrata who invited him to Pavia to hold some academic lessons. The Italian hematologist then asked him to host Introzzi in Berlin for a period of training. I got this information from Peter Schwartz, former Professor of Cardiology in Pavia and cousin of Zoltan Alexander Leitner.*

name is linked to De Toni-Fanconi-Debré syndrome), who investigated the possible relationship between Jennerian vaccination and the alterations of hematopoiesis.[102]

In the '30s, *Haematologica* continued to host articles also from various foreign countries, including the United States (Harvard University and Jefferson Medical College of Philadelphia).[103-110] The journal was at that time the fundamental forum for activities related to hematology in Italy and in 1935 became the official journal of the Italian Society of Hematology, publishing its acts, statutes and regulatory guidelines.

In 1940, with Europe thrown into the turmoil of the Second World War, *Haematologica* celebrated its twentieth anniversary with an impressive volume in honor of the founder Adolfo Ferrata, promoted by his most illustrious pupil Di Guglielmo. Di Guglielmo undersigned the introduction, dedicated with great affection to his teacher, and was himself the author of an extensive study of the pathology of the spleen.[111] Of course, the war completely interrupted the flow of scientific contributions from abroad. Among the many works that came from Italy, one stood out clearly and was signed by Edoardo Storti with his collaborator Mario Brotto (who had graduated just two years before).[112] It was a statistical and clinical-pathological study of 157 cases of leukemias which clearly took a position in favor of the old hypothesis, sustained between the nineteenth and the twentieth centuries by Hugo Ribbert (1855-1920), Guido Banti (1852-1925) and other pathologists, that leukemias were neoplastic diseases, in stark contrast to the view presented by Ferrata, Otto Naegeli (1871-1938), and other clinicians who instead claimed them to be hyperplastic illnesses. This testifies to the liberal atmosphere that so characterized the Pavia Medical Clinic and the original *raison d'être* of *Haematologica* directed by Ferrata, who, in honor of the freedom of research, allowed one of his pupils to advocate ideas diametrically opposed to those he himself supported. The topic was

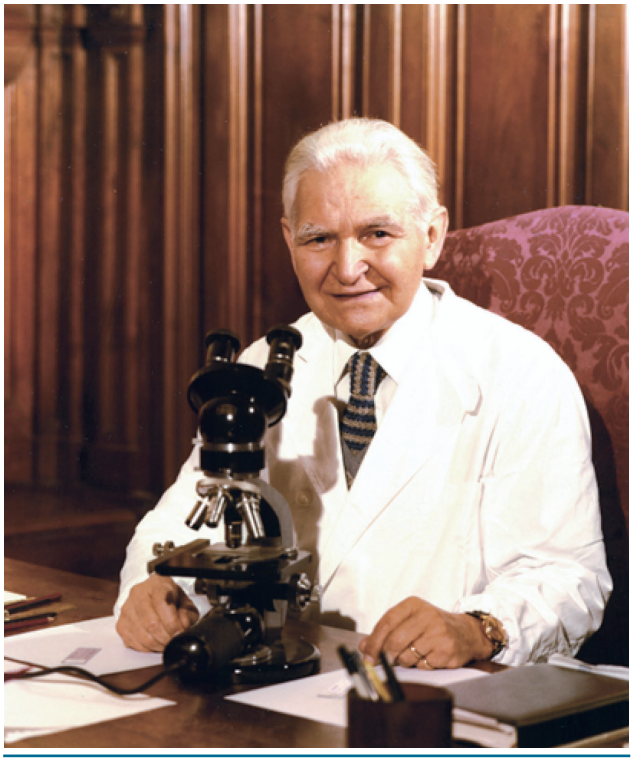

Figure 7. Edoardo Storti.

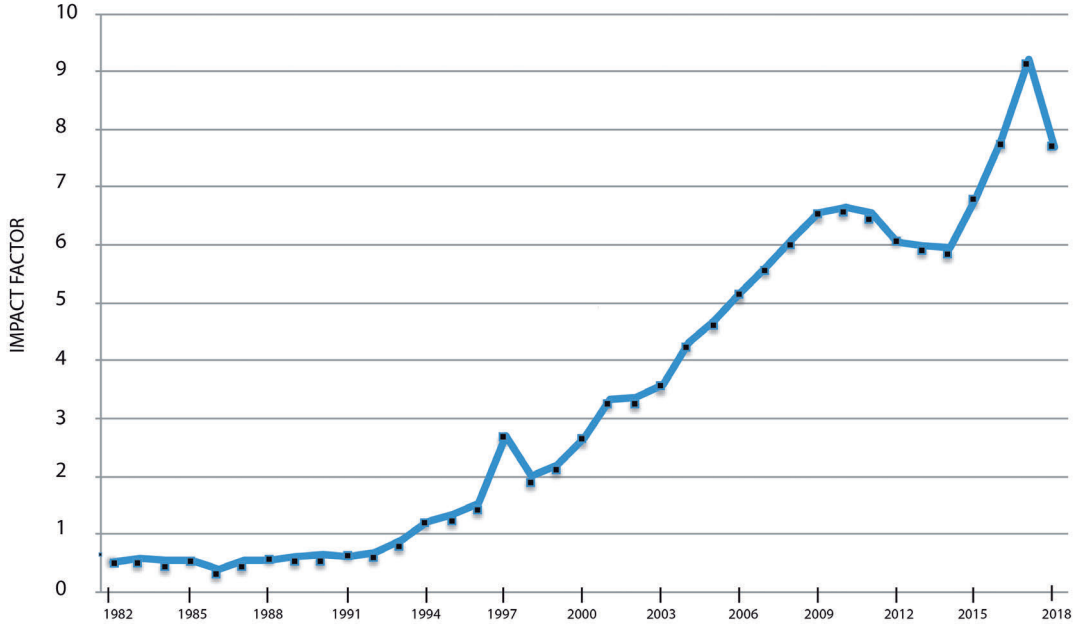

Table 1. *Haematologica Impact Factor for the years 1982-2018.*

immediately discussed in the following months,[113] and very soon the idea of the neoplastic origin of leukemias became a fact adopted by the international community of hematologists.

In the following years, the journal continued to publish significant works on many areas of blood morphology and pathology, for example, on the relationship between pulmonary tuberculosis and hematopoiesis,[114,115] in splenectomy in aplastic myelosis,[116] on a form of familial leukemia,[117] on chronic erythremic myelosis,[118] and others. The number of articles was, however, drastically reduced, and there were no published contributions from foreign research centers.

Ferrata died suddenly in 1946, and the direction of *Haematologica* was assigned to Giovanni Di Guglielmo (from 1946 to 1960) and then to Paolo Introzzi (from 1961 to 1973). However, the negative trend steadily continued and the decline also affected the other traditional European hematologic journals, like *Blut, Folia haematologica*, *Le sang*, that stopped publishing and disappeared from the scene. At the beginning of the '70s, *Haematologica* had only about a hundred subscribers divided between libraries and Italian hematologists, mostly related to the Ferrata school. This was the editorial situation in 1973 when Edoardo Storti became president of the Italian Society of Haematology and director of the journal.

A second beginning

Storti decided that it was worth attempting to revive the magazine and co-opted his pupils Sergio Perugini (1925-1979) as Assistant Editor and Edoardo Ascari as Scientific Secretary.[119] With a respected publisher, "Il Pensiero Scientifico Editore", which could ensure the continuity and regularity of publication, the new adventure began. From the beginning, Storti decided to promote the diffusion of the journal on the national and international stage, trying to increase the number of articles published in English, or, at least, to always provide a summary of the work in English. The journal management selected some Italian and foreign hematologists to ensure a rigorous and proper peer review of the articles submitted. Having taken these first steps, and seeing the credibility of the journal subsequently increase, from 1978, *Haematologica* was placed under an observation procedure by the Institute of Scientific Information. Its bibliometric impact, however, was initially very low.

In 1983, Storti, in agreement with the heirs of Ferrata, gave birth to the "Ferrata Storti Foundation", becoming its first president, and providing it with a substantial financial endowment. Its purpose was "to promote and encourage studies and research on blood diseases and their treatment".[120,121] One of the aims of the Foundation was "the support and the strengthening of *Haematologica*", which in the meantime had become the oldest surviving journal on blood diseases. Meanwhile, the number of articles coming from abroad was steadily increasing. Ferrata's heirs, who were the owners of *Haematologica*, donated it to the Ferrata Storti Foundation, and from 1985, the journal began to be published completely in English. In 1990, Storti passed the role of Editor to Edoardo Ascari with Mario Cazzola as Assistant Editor. At the same time, the journal was elected as the official organ of the Italian Society of Hematology and, since 1997, also of the Spanish Society of Hematology and Hemotherapy. Mario Cazzola became Editor of the journal in 2002 and, thanks to the endeavors of Emili Montserrat and Robin Foà, in 2005, *Haematologica* became the official organ of the European Hematology Association.[122] In that same year, Robin Foà became co-editor of the journal with Cazzola, joined by a team of 12 Associate Editors.

Ever since *Haematologica* has been published online, the management of the magazine and the Ferrata Storti Foundation have adopted the Open Access publishing mode. In the '80s and '90s, the Impact Factor (IF), which by the first evaluations was very low (in 1982 it was 0.409), grew slowly but steadily,[123] then to increase strongly in the first decade of the new century, thanks also to the commitment of Cazzola during the period of his management of the journal between 2002 and the end of 2011.

From the first of January 2012, Jan Cools was appointed Editor-in-Chief of *Haematologica* with Luca Malcovati as Deputy Editor. The Ferrata Storti Foundation has continued to promote and financially support the journal under the presidency of Edoardo Ascari (since 2002) and subsequently of Carlo Balduini. The last change in management of *Haematologica* came in 2018, when Luca Malcovati became Editor-in-Chief.

The last twenty years have seen a major transformation of the journal and it has become a reference point for studies in every field of hematology. All those who have contributed to making *Haematologica* great in the past hundred years, thanks to the scientific contributions they have made to the journal, have laid the foundations for an equally radiant second centenary.

A great past is the hope for an equally great future.

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