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History

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50th Anniversary of *Clinical Chemistry and Laboratory Medicine* – a historical overview[1)]

Abstract

In the early 1960s, *Joachim Brugsch*, one of the founders of *Clinical Chemistry and Laboratory Medicine* (*CCLM*) (then *Zeitschrift für Klinische Chemie*), had the idea to found a journal in the upcoming field of clinical chemistry. He approached *Ernst Schütte*, who was associated with the De Gruyter publishing house through another journal, to participate, and *Schütte* thus became the second founder of this *Journal*. The aim was to create a vehicle allowing the experts to express their opinions and raise their voices more clearly than they could in a journal that publishes only original experimental papers, a laborious and difficult, but important endeavor, as the profession of clinical chemistry was still in the early stages of development at this time. The first issue of this *Journal* was published in early 1963, and today, we are proud to celebrate the 50th anniversary of *CCLM*. This review describes the development of this *Journal* in light of the political situation of the time when it was founded, the situation of the publisher Walter De Gruyter after the erection of the Berlin Wall, and the development of clinical chemistry, and later on, laboratory medicine as a well-acknowledged discipline and profession.

Keywords: *Clinical Chemistry and Laboratory Medicine;* development; history.

[1)]For name changes throughout the years, refer to Table 1 in reference [22].

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Preliminary remarks

In his article 'The Foundation of the German Society of Clinical Chemistry' [1], *Dankwart Stamm* (1924–1994) notes: 'The report is based on the publications and documentation of that time. Where such documents do not accurately reflect the situation, especially the difficulties and motivations of those involved, we have made our own contributions from memory', from correspondence and literature, 'to show the tensions surrounding the foundation of the Society.'

The author uses this statement also for his explanations in the article.

As for mentioning persons as well as their words and actions, we assume that data protection is not relevant after 50 years, particularly as most of those involved at that time are no longer with us.

The establishment of *Clinical Chemistry and Laboratory Medicine* (*CCLM*), then *Zeitschrift für Klinische Chemie*, must be understood in the context of the people acting at that time, the situation of the publisher, as well as the political and economic historical circumstances of Berlin. This is why these aspects will be addressed first.

This applies equally to the selection of the members of the scientific advisory board, which reflects the polarity between the two founding editors.

The majority of the citations in this article are translations from German language sources. Citations that are not referred to in the reference list are from correspondence between the parties involved in the foundation and development of this *Journal*.

Friedrich Körber compiled the first part of this 'look back' from his experience of 30 years (1967–1997) acting as Managing Editor; the second part was written by *Mario Plebani*, appointed to the Editorial Board of *CCLM* in 2002, *CCLM*'s Reviews Editor between 2006 and 2008, and Editor-in-Chief of the *Journal* since July 2008.

The political situation of the city of Berlin at the beginning of the 1960s

At the end of 1958, the Soviet Union, under *Nikita S. Khrushchev*, sent a note to the three Western Allies, in which he demanded that Berlin (West) was to be demilitarized and turned into a Free City, thus giving expression to the 'three-state theory'. The three Western powers and the German federal government rejected *Khrushchev*'s ultimatum, which expired without any results. The 'three-state

theory' of the Eastern bloc referred to 'West Berlin' as a special political unit. Berlin (West) was surrounded by East Berlin and the territory of the German Democratic Republic (GDR), and there were agreements by the Allied Forces for border crossings within the city of Berlin, from the GDR to 'West Germany', as well as air and road corridors to the 'West', i.e., the Federal Republic of Germany.

The state officials of the GDR increasingly subjected cross-border workers who lived in the East and worked in the West for a partial wage in 'Western money' to repressive measures.

On August 13, 1961, the erection of the Berlin Wall surprised everyone. It served to seal off the East of Germany from Berlin (West), and the stream of refugees from the GDR to the West was stopped. Students from the GDR, who had been able to pursue their studies unhindered, together with myself, at the Free University of Berlin, had to discontinue their studies. Engaged couples were torn apart, something that also affected the author briefly. However, there were also border crossers in the opposite direction, e.g., doctors who lived in Berlin (West) but worked in East Berlin. They were allowed to continue crossing the border.

After the building of the Berlin Wall, when GDR officials tried to limit the rights of the Allied powers in Berlin, all hell broke loose at the sector border crossing 'Checkpoint Charlie', in Friedrichstrasse: Soviet and American tanks were facing each other on October 27, 1961, ready to fight [2].

It is only against such background that the following episode can be understood: *Cecil James Watson* (1901–1983), who had been asked by *Joachim Brugsch* (1909–1980) about his participation in the *Journal*, rejected the offer without any explanation. *Richard Duesberg* (1903–1968) agreed to mediate, and thus communicated to *Joachim Brugsch* the following reply from *C.J. Watson*: 'With respect to the matter of *Brugsch*-Berlin and the *Zeitschrift für Klinische Chemie*, may I ask you, in all confidence, whether *Brugsch* is in East Berlin or West Berlin? If the *Zeitschrift* is published in West Berlin and is definitely not under any possibility of Communist influence I would be quite pleased to have my name included, but I would appreciate a word from you first about the questions that I have raised.'

C.J. Watson then wrote to *Joachim Brugsch*: 'As Professor *Duesberg* has indicated to you, one of my reasons for previously declining to serve on the Scientific Board of the *Zeitschrift für Klinische Chemie* was that I thought this might be published in East Berlin. Evidently I had been misinformed about this by a German physician who is here. He indicated to me that a number of the addresses were in East Berlin. I would be willing to accept your kind invitation if you will assure me that the *Journal* is not published in East Berlin and that there is no business or professional relationship of any kind with East Berlin. If this were true I would have to decline. I felt quite certain that you were not Communist but I did not know whether others related to the *Journal*, or the publishers thereof, were and I must be fully assured on this point.'

In October 1962, *Joachim Brugsch* assured him 'that the publisher of the *Zeitschrift für Klinische Chemie* edited by me, Walter de Gruyter & Co, has been domiciled in West Berlin as a strictly scientific publishing house since its foundation. I can also assure you that this company is, of course, beyond any doubt politically speaking. Your assumptions, therefore, do not apply at all, and I am happy to be able to tell you this. I hope this information will dispel any doubts. I enclose an overview of the members of the scientific advisory board of the *Zeitschrift für Klinische Chemie*, which shows that not even one East Berliner will be employed by us. This, too, should afford you peace of mind. I have not been active in East Berlin for over a year, and now work as a chief physician in West Berlin. I, therefore, ask you again for your permission to include your name among the members of the scientific advisory board of the *Zeitschrift für Klinische Chemie*.'

And this is what happened, and *C.J. Watson* contributed a lengthy article titled 'On acute intermittent porphyria' [3].

The publishing house Walter de Gruyter (Berlin West) in the post-war years [4]

Lost connections with authors due to the war, the 'harsh winter of 1946/47, the currency reform of 1948, and the blockade of Berlin by the Soviets in 1948/49 severely limited the activities of the publisher. ... The sales from reprints and the sale of old stock became the basic business of the modern publisher Walter de Gruyter.' In the case of De Gruyter, this included primarily the Clinical Dictionary by *Willibald Pschyrembel* (1901–1987), a member of the scientific advisory board of the *Zeitschrift für Klinische Chemie*, as well as textbooks on mathematics and natural science, and various small volumes from the Göschen collection.

The consistent use of old publishing rights launched a consolidation process. An external sign of the stabilization was, in 1960, the commissioning of a new printing press in Genthiner Strasse 5–9. The composing room, too, which had been housed tentatively at the publisher's building since 1949, was located there. In 1980, the printing press was spun off under the name Arthur Collignon GmbH, but it remained the sole property of De Gruyter.

The construction of the Berlin Wall in 1961 also divided the staff of the De Gruyter publishing house. About one-third of the printers and typesetters were no longer able to show up for work. This necessitated a complete reorientation of the business policy towards the Federal Republic of Germany and countries of the West.

For a long time, the lack of financial resources and staff made it impossible to develop a new program. It could only focus on a few areas, medicine and law. It was not until the 1960s that De Gruyter was again in a position to handle projects that would live up to the reputation of the publishing house.

It was then that *Joachim Brugsch* and *Ernst Schütte* contacted the publisher's Department of Medicine headed by *Hans-Joachim König* (1903–1971), and agreed, in spring 1962, to launch the *Zeitschrift für Klinische Chemie*. It was supposed to be published for the first time in autumn 1962.

The founders of the *Journal*

The professors *Brugsch* [5, 6]

The specialist for internal medicine *Theodor Brugsch* (1878–1963) was appointed Professor and Director of the Medical Department in Halle/Saale in 1927.

His three sons were also medical doctors:

1. *Heinrich* (1903–?), who lived in the US;
2. *Herbert* (1905–1972), at whose children's clinic, at the city's hospital Moabit in Berlin, the author completed as a student an internship in the second half of the 1950s; and
3. *Joachim* (1909–1980), whom I would later, when I was the Managing Editor of this *Journal*, meet in his capacity as the founder of the *Zeitschrift für Klinische Chemie*.

Theodor Brugsch, Halle/Saale, got into trouble with the National Socialists after 1933 when they had classified his wife as a Jew. In 1935, this forced him out of his position. His sons, active at the Department of Internal Medicine and at the children's clinic, were dismissed as 'first-degree half-breeds' and persecuted for being Jewish.

Joachim Brugsch graduated from the Prince Heinrich secondary school at Easter 1926 and completed medical school in Halle in 1932, where his father was Department Director (see above), 'summa cum laude'.

In his curriculum vitae, *Joachim Brugsch* wrote on November 20, 1949: 'My scientific education I obtained at the University Teaching Hospital in Halle … that is, from 1933 to 1935; in 1935–1936, I worked at the Westend sanatorium. In 1936/37, I went to the Mayo Clinic as a researcher, returning to Germany in 1937, where I continued to practice medicine and conducted scientific research: I was barred from holding a position at the clinic due to National-Socialistic decrees, which explains my decision to work at the Mayo Clinic. From 1939, I was forced to continue my work at a private laboratory, and was allowed to work as a general practitioner only for the time being.'

In Berlin, both sons were granted residential permits – *Herbert* in Charlottenburg and *Joachim* in Tiergarten, but only as general practitioners until further notice. As the war wore on, both doctors were conscripted, *Herbert* as a surgeon's assistant in Dinslaken, while *Joachim* was deployed with the Red Cross in East Germany.

After the end of World War II, *Joachim Brugsch* applied in summer 1945 to the Medical Clinic (Director: *Gustav von Bergmann* [1878–1955]) of the University Hospital Charité.

However, since this required him to give up practising, he went to the First Medical Clinic of Charité where his father, *Theodor Brugsch* (see above), had been a director. *Joachim Brugsch* started his position there as of September 1, 1945. On January 26, 1946, he was given a teaching assignment for clinical chemistry at the recently opened Berlin University.

On April 9, 1946, he submitted his habilitation application for internal medicine to the interim dean of the medical school, *Karl Lohmann* (1898–1978), a physiological chemist. The title of his thesis: 'Studies on the significance of the tetrapyrrole system in the human pigment metabolism'.

His thesis advisors were *Karl Lohmann* himself and the pharmacologist *Wolfgang Heubner* (1877–1957). The latter explained, among other things: 'That this involves only previous, and already published, studies may be blamed on the external circumstances of the last few years.'

In July 1947, *Joachim Brugsch* succeeded *Walter Seitz* (1905–1997), a member of the scientific advisory board of the *Zeitschrift für Klinische Chemie*, and became senior physician at the Charité clinic headed by his father in Berlin.

In November 1947, he advanced to Director of the Clinical-Chemical Department of the First Medical Clinic of Charité. Recognition as a specialist of internal medicine followed in 1950. In 1952, *Joachim Brugsch* was promoted to Professor for Internal Medicine by the State Secretary of Higher Education in the GDR, and became Deputy Director at the clinic headed by his father (!).

At the City Hospital in Berlin-Friedrichshain, the 'people's uprising' on June 17, 1953, resulted in the departure of the Director of Internal Medicine, Dr. *Paul Rössing* (1911–1990) – at age 42.

On May 1, 1954, *Joachim Brugsch* assumed the position of chief physician of the Department of Internal Medicine of that hospital. He was allowed to use the laboratory of the First Medical Clinic of Charité, and was also assigned a laboratory assistant, a privilege that he would likely take advantage of for several years.

He would have a full schedule every day:

- at the Charité laboratory in the morning;
- chief physician at the clinic and polyclinic during the second half of the morning and other parts of the day;
- in the afternoon, his practice in Levetzowstrasse 19 in Berlin-Moabit, which is still being run by his son *Alexander* today;
- literary work in the evening.

On August 13, 1961, the Berlin Wall was put up. In the late summer of 1961, his position at the City Hospital Friedrichshain was terminated. The reasons for this are unknown.

In Berlin (West), *Joachim Brugsch* first had nothing but his practice in Moabit (see above). He decided to accept the position of chief physician at the private clinic 'Lindenhaus' in Berlin-Dahlem. In 1970, he became Director of the denominational Theodosius Hospital in Berlin Lankwitz, where, again, he had a laboratory at his disposal.

The establishment of a center for porphyria patients, planned by *Joachim Brugsch* and which was also to include running family case histories, failed due to the fact that the clinic of the hospital was shut down. It appears, however, that he remained its senior physician until his death on November 18, 1980.

Prof. Dr. med. Dr. rer. nat. *Ernst Schütte*

The work that *Ernst Schütte* did for physiological chemistry, biochemistry and clinical chemistry has been recognized by this, 'his' *Journal*, repeatedly [7–11].

I quote from the obituary I wrote as Dean for the Newsletter of the Free University of Berlin [12]: 'Born into a doctor's family on June 14, 1908, he graduated from high school to go on to Bonn, Munich and Berlin to study medicine and chemistry. In 1935, he completed his doctorate in medicine in Berlin and in 1942, his doctorate in natural sciences in Leipzig. With *Karl Thomas* (1883–1969) as his advisor, he obtained his habilitation in Leipzig, worked at the Military Medical Academy in Berlin during the final years of the war, and in 1946, he obtained his habilitation in Frankfurt am Main in physiological and clinical chemistry. It was there that he headed the clinical-chemical laboratory at the teaching hospital under *Franz Volhard* (1872–1950).

He returned to Berlin in 1950 as a Guest Professor of physiological chemistry, and in 1951 accepted a professorship and position as Director of the Department of Physiological Chemistry at the Free University of Berlin. He built his department and specialization, where he worked on nutrition and the metabolism of water, salt and bones, from simple beginnings at the building in Lentzeallee 75, which belongs to the Agriculture Department of the Technical University of Berlin, where he was also an Honorary Professor.

Almost half his time spent working at that university had passed until in 1963 the department building in Arnimallee was completed, thus finally giving him the working conditions he had been promised. There, he dedicated his entire work to improving the practical training of medical students in physiological chemistry [13]. He educated and examined a whole generation of future doctors in physiological chemistry. Most of his co-workers became university teachers, some in the US, others in Germany, including in Berlin.

For several years, *Ernst Schütte* was Secretary and, from 1960 to 1962, President of the Society of Physiological Chemistry (today: Society of Biochemistry and Molecular Biology). Together with *Kurt Felix* (1888–1960) he laid the foundation for the establishment of a diploma in clinical chemistry, initially through the Society of Physiological Chemistry. It is to his commitment that we owe the establishment of one of the first chairs in clinical chemistry in Germany at the Steglitz clinic of the Free University of Berlin. Similarly, he worked with *Günter Hillmann* (1919–1975), *Eugen Werle* (1902–1975), and *Hansjürgen Staudinger* (1914–1990) to set up an independent German Society of Clinical Chemistry when he realized that building out the discipline of clinical chemistry at the then international level of science was possible in Germany, only if it was set up as an independent subject and integrated with training in clinical medicine, and if those involved in the subject were members of a separate scientific society for exchanging ideas and representing their common interests.

Together with *Joachim Brugsch*, he founded the *Zeitschrift für Klinische Chemie* in 1963. He acted as Editor-in-Chief for 23 volumes up to his death, and was particularly committed to the development of clinical biochemistry and pathobiochemistry.

For his services in the development of clinical chemistry as a separate discipline in Germany, he was the first to be awarded the Johann Joseph Scherer Medal created by *Gerhard Marcks* (1889–1981) [10] by the German Society of Clinical Chemistry on June 29, 1978 [10].

Soon after his retirement in 1976, *Ernst Schütte* made Markgräflerland his new home and enjoyed the rural lifestyle, without losing contact with his colleagues and

science: to his final days, he would actively participate in meetings of 'his' scientific societies.

He died on May 8, 1985, in Hertingen (Bad Bellingen), where he was laid to rest on May 13, 1985.'

The situation of clinical chemistry in Germany at the beginning of the 1960s and the umbrella of international bodies

Ernst Schütte and *Johannes Büttner* (born 1931) provided a detailed account of the situation of clinical chemistry in their birthday address for *Eugen Werle* [14; see also 15, 16]:

'In 1955 clinical chemists, at the instigation of *Karl Hinsberg* (1894–1982), formed an association ... within the 'Society of Physiological Chemistry'.' The local court in Frankfurt/Main, which was responsible for the register of associations, rejected the establishment in the bylaws of a section for clinical chemistry.

Thus, an interim solution was applied for a while, with different committees within the Society:

- the 'Standing Committee of Clinical Chemistry', first presided over by *Karl Hinsberg*, followed in 1959 by *Eugen Werle*;
- the 'Committee for the Drafting of Guidelines for the Training of Clinical Chemists';
- and the Committee for the granting of a 'Diploma as Clinical Chemist'.

However, this way, it was impossible to create a national and international representation.

The biochemists and, thus, also the Society of Physiological Chemistry were organized internationally as part of the IUB, while clinical chemists found a home in the Commission on Clinical Chemistry of IUPAC. IUPAC, however, could not accept representation of German clinical chemists by an association of IUB, that is, the Society of Physiological Chemistry. So, it transpired that German Clinical Chemistry was not represented by its own association within its international umbrella organization. If there was any representation at all, it was through *Eugen Werle* himself, who had been a member since 1959 as holder of the first, and for some years, only chair of clinical chemistry at German universities, and since 1962, in recognition of his scientific accomplishments, as a National Representative of the Commission on Clinical Chemistry of IUPAC.

Thanks to his personal commitment, *Werle* managed in Detroit in 1963 to convene the 6th International Congress of Clinical Chemistry in Munich in 1966. At once, he provided a key impetus for the further development of clinical chemistry in Germany, for it was clear that an appropriate German representation of the discipline as a separate institution was necessary for such international congress.

International Union of Biochemistry (IUB)/ International Union of Biochemistry and Molecular Biology (IUBMB) [17]

The International Union of Biochemistry (IUB), now International Union of Biochemistry and Molecular Biology (IUBMB), founded in 1955, unites biochemists and molecular biologists in 77 countries. The union is devoted to promoting research and education in biochemistry and molecular biology throughout the world. It achieves this in several ways.

'The International Federation of Clinical Chemistry and Laboratory Medicine, as well as other bodies are also Associated Organisations of IUBMB. Reaching individual biochemists is also the purpose of another very important function of the IUBMB, that of publishing news, reviews, information, original research and nomenclature.'

Well-known and important publications are:

- Recommendations (1964) of the International Union of Biochemistry on the nomenclature and classification of enzymes. (847 entries)
  Later on published as
- Enzyme Nomenclature, Recommendations (1972) of the International Union of Pure and Applied Chemistry (IUPAC) and the International Union of Biochemistry (IUB) Elsevier Amsterdam 1973. (1770 entries)
- Enzyme Nomenclature, Recommendations (1978) of the IUPAC and the IUB Academic Press New York etc. 1979. (2122 entries)
- Enzyme Nomenclature, Recommendations (1984) of the IUPAC and the IUB. Academic Press New York etc. 1984. (2477 entries)
- Enzyme Nomenclature, Recommendations (1992) of the IUPAC and the IUB
  Academic Press New York etc. 1992. (3196 entries)

International Union of Pure and Applied Chemistry (IUPAC) [18]

The International Union of Pure and Applied Chemistry (IUPAC) serves to advance the worldwide aspects of the chemical sciences and to contribute to the application in the service of mankind.

IUPAC was formed in 1919 by chemists from industry and academia, who recognized the need for international standardization in chemistry. The standardization of weights, measures, names and symbols is essential to the well-being and continued success of the scientific enterprise and to the smooth development and growth of international trade and commerce.

IUPAC has long been recognized as the world authority on chemical nomenclature, terminology, standardized methods for measurement, atomic weights and many other critically evaluated data.

This desire for international cooperation among chemists and facilitation of the work of the international, but fragmented, chemistry community were the earliest characteristics of the Union. Even before the creation of IUPAC (1919), a predecessor body, the International Association of Chemical Societies (IACS), had met in Paris in 1911 and produced a set of proposals for the work that the new Association should address. These included:

- Nomenclature of inorganic and organic chemistry;
- Standardization of atomic weights;
- Standardization of physical constants;
- Editing tables of properties of matter;
- Establishing a commission for the review of work;
- Standardization of the formats of publications;
- Measures required to prevent repetition of the same papers.

IUPAC serves the international scientific endeavor in the dual function of a basic science and a mission-oriented Union.

Another well-known and important publication appeared after its first edition 1973:

Collected Tentative Rules and Recommendations of the Commission on Biochemical Nomenclature IUPAC – IUB and Related Documents, second edition 1975, Reprinted (1975) by the American Society of Biological Chemists, Inc., Bethesda, USA.

A third volume has been prepared for the International Union of Biochemistry by its Committee of Editors of Biochemical Journals, supported by IUPAC – IUB Biochemical Nomenclature and Related Documents, Reprinted (1978) by Spottiswoode, Ballantyne Press for the Biochemical Society, London.

International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) [19]

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) has existed since 1952.

The initial objectives of the Federation were to 'advance knowledge and promote the interests of biochemistry in its clinical (medical) aspects'. In the early years, IFCC was closely associated with the IUPAC Commission (later Section) of Clinical Chemistry, and initially, the Committee of IFCC comprised of members of the IUPAC Commission. It was recognized, however, that the IFCC should become independent, but would retain its contact with the IUPAC through affiliation as an Associate Member. This was accomplished in 1967, when the two organizations were formally separated.

The IFCC is also working with a number of other international organizations such as:

- the Institute of Reference Materials and Measurements (IRMM);
- the National Institute of Standards and Technology (NIST);
- the National Committee for Clinical Laboratory Standards [NCCLS (now known as the Clinical and Laboratory Standards Institute (CLSI)];
- the Bureau International des Poids et Mesures (BIPM)

in developing the standards and in the area of standardization of methods. Standardization on high metrological levels has always been a major undertaking and has contributed to the credibility of IFCC. The IFCC continue to be very influential in defining and reviewing appropriate terminology in Laboratory Medicine and other fields of chemistry.

The IFCC is now a Federation of 88 Full Member National Societies of Clinical Chemistry and Laboratory Medicine representing about 45,000 individual clinical chemists, laboratory scientists, and laboratory physicians, and 49 Corporate Members covering the major areas of clinical laboratory developments.

Members of the bodies and friends of this *Journal* held important positions in the IFCC: In 1976, Dr. *Jörg Frei* was elected President after an 8-year period as secretary. Dr. *René Dybkaer* followed him in 1979 after 6 years as Vice-President. Dr. *Donald Young* became President in 1985, after a 3-year term as Vice-President. During his 6 years as President, Dr. *Young* reorganized the committee structure of the IFCC. Professor *Gérard Siest* was President from 1991 to 1996. From 1997 to 1999 the President was Professor *Matthew McQueen* who was previously a member of the Scientific Committee from 1982 to 1987, Treasurer from 1989 to 1990 and Vice President 1991 to 1996. One highlight of the late 1990s was the very important name change to the International Federation of Clinical Chemistry and Laboratory Medicine, highlighting the clinical relevance and importance of our profession. Professor *Mathias M. Müller* served as President for the period 2000–2005. He

also served the Federation as Secretary and Vice-President, and Vice-chair and Chair of the scientific division. Professor *Jocelyn Hicks* served as President from 2005 to 2008. Dr. *Graham Beastall* has been President of the IFCC since 2009 [19].

The *Zeitschrift für Klinische Chemie* adopted the recommendations of those bodies and integrated them into its recommendations for the drafting of manuscripts, which were first updated comprehensively in 1972, in volume 10, pp. 294–307, and have been updated regularly since then.

This *Journal* has published regularly the recommendations of the IFCC since 1975. The Cumulative Index 1(1975) – 1989/2 was published in 1989, in volume 27, pp. XXXVII–LXII.

The founding of the *Zeitschrift für Klinische Chemie* and its first volume

Editors – scope – Editorial Board

Joachim Brugsch was the one to have initiated this *Journal*. From the very beginning, he was among the editors, until 1974 as Editor-in-Chief. His involvement ended with his death in 1980 [20, 21].

Joachim Brugsch brought aboard *Ernst Schütte*, Professor of Physiological Chemistry at the Free University of Berlin since 1951 (see also Table 2 in [22]).

In late May 1962, *Ernst Schütte* wrote to *Eugen Werle*: 'As you can see from the letterhead, I have become one of those editors of more or less superfluous journals. The story is this: the internal medicine specialist *Joachim Brugsch*, who had worked with *Hans Fischer* and/or *Karl Zeile* in Munich for a few years, as well as in the field of porphyrins and in internal medicine, must have had the original idea and taken it to the De Gruyter publishing house, with which I am associated through *Hoppe-Seyler* and which asked me to participate. The plan is not for a journal along the lines of the journals *Hoppe-Seyler* or *Biochemische Zeitschrift*, etc., but rather more like the journal *Angewandte Chemie*. In other words, a vehicle that allows the editors to express their opinions and raise their voices more clearly than they could in a journal that publishes only original experimental papers. Especially from the current situation of clinical chemistry, it seemed important to me to be represented in such undertaking, rather than the 'specialist doctors of laboratory medicine'. This was one of the essential reasons why I eventually accepted the offer.'

On the same date, he wrote to *Horst Frunder* (1919–2012), Jena: 'As you can see from this representative letterhead, I have become one of those editors of superfluous medical journals. But since it was the De Gruyter publishing house, and the request was expressed rather urgently, I have accepted the offer, not least to prevent worse from happening.'

The *Zeitschrift für Klinische Chemie* was given its name [see also Table 1 in [22]] in analogy to the *Zeitschrift für Physiologische Chemie*, published by the same publishing house in 1877 and founded by *Felix Hoppe-Seyler* (1825–1895). Both journals changed their names and appearance several times, for reasons of substance and scientific policy but also for alphabetical reasons (based on its German title), e.g., so as not to be listed near the end of the 'Bibliographic Guide for Editors and Authors' (published in 1974 by The American Chemical Society, Washington, DC).

We do not know about the arrangements made between *Joachim Brugsch* and *Ernst Schütte* and Walter de Gruyter publishers. At any rate, the spring of 1962 saw the start of intense correspondence. All three involved, as well as the Managing Editor Dipl.-Chem. *Günter Eugen Halder*, did try, in the correspondence, to achieve a scientific advisory board of international members and attract authors. In early May 1962, *Joachim Brugsch* wrote to his brother *Heinrich* in the US: 'For the first six issues of the *Journal*, we have worked out the following editorial content on a tentative and private level:

I. a. 'Lipoid chemistry' (Thannhauser issue)
   b. 'Blood sugar'
II. a. 'Warburg method' (Warburg issue)
   b. 'Uric acid'
III. a. 'Proteohormones' (Zondek issue)
   b. 'Cation analysis'
IV. a. 'Steroid chemistry' (Windaus issue)
   b. 'Non-protein-N procedures'
V. a. 'Liver therapy' (Murphy-Castle issue)
   b. 'Enzymes of glycolysis'
VI. a. 'Protein chemistry' (Hans Fischer issue)
   b. 'Polarography'

The 'dedications' in parentheses indicate the lack of the future-oriented character of the planned *Journal*, instead creating a 'historical' impression. It is not all that different with respect to the international members recruited for the scientific advisory board:

Represented:
- Germany (West) 28
- USA 6

– Switzerland 5
– Sweden 2
– Austria 1

By discipline:
– Clinicians 18
– Biochemists 13
– Clinical chemists 5
– Non-specific 2
– Veterinarians, physicists, gynecologists, pharmacologists, 1 each

…. only men, primarily of more advanced age. A source of potential conflict!

Even before the *Journal* was published, *Nepomuk Zöllner* (born 1923), member of the scientific advisory board, wrote to *Joachim Brugsch*: 'It is striking that your scientific advisory board includes a number of people who have never held a test tube in their hands and who have never stood out in terms of publication, be it as a chemist, or as a clinician. I do understand that one requires a number of figureheads, but why you should have chosen hematologists, cardiologists and angiologists is something I cannot understand. What is more, given the relatively lopsided selection from the large clinical field, the *Journal* has an imbalance in internal medicine, which may be a hindrance to its development. In short, insofar as I may counsel you, I would like to recommend that, on the occasion of the departure of one or the other member of your board, you should give preference to clinicians with experimental experience that allows them to make positive contributions.

The excess of non-expert clinicians is matched by a deficit of existing reputable clinical chemists. Aside from *Benno Hess*, who is the most recent cause giving rise to this letter, one should mention Professor *Werle* here in Munich, who is the only full Professor of Clinical Chemistry in Germany, and Dr. *Hillmann* in Tübingen, who heads the large laboratory at the clinic by commission of the Ministry, and who has stood out with research of his own and who may be an excellent and critical conversation partner, albeit not an easy choice for everyone.'

At the end of May 1964, *Ernst Schütte* wrote to *Einhart Kawerau*: 'I am working to activate the scientific advisory board insofar as it can be activated. Some of the names printed on our cover sheet are, of course, purely representative, as is customary among German scientific journals – and certainly not to their benefit.'

The publishing house and editors filled a folder with correspondence with members of the advisory board, as well as with potential authors selected by them. When writing to the individual recipients, they took turns frequently, canvassing vehemently for manuscripts. The publishing house even prepared brochures for this purpose.

In a foreword, signed by hand by *Joachim Brugsch*, dated April 1962, accompanied by a note 'to be published in fall 1962', it is written: 'This *Journal* is to promote the development of clinical chemistry in the German-speaking regions through summary overviews as well as basic and critical accounts of the necessary premises. In this context, one only needs to remind the experienced reader of his own wealth of historical fundamentals. International cooperation, which goes without saying, and teaching as a basis for clinical chemistry are prerequisites for this *Journal*'s thriving and development. But such development, we hope, is to be achieved through the intense scientific participation of clinicians, researchers and practitioners and to be reflected in their results, which should be transparent, concise and exhaustive.'

Another brochure signed by the editors and publisher provided this incisive summary:

'The *Zeitschrift für Klinische Chemie* has been founded by the editors to close a gap in the German literature that has been noticed for years. So far, there has been no journal in German-speaking regions that looks at the vast field of clinical chemistry critically and comprehensively. Thus, one often finds excellent clinical-chemical papers scattered across major general-medical journals, where they are not as noticed as they should be. With this *Journal*, the editors wanted to allow doctors and chemists who worked as clinicians, practitioners or for an institution to inform themselves, quickly and comprehensively, about advances in the overall field of clinical chemistry. Accordingly, the author can publish his findings within a short amount of time and disseminate them to specialist colleagues with a special interest.

The *Zeitschrift für Klinische Chemie* will attempt to provide as comprehensive an account of the current state-of-the-art development and research in all areas of clinical chemistry. This means that the classical chapters of physiological chemistry will be used to discuss and interpret the variety of problems in clinical chemistry. In addition, the special primary aspects of chemical research in the clinical and practical fields will be emphasized. The detailed description of new and improved work methods at the clinical laboratory will be given special attention, because the value, or non-value, of a study depends decisively on the reliability and accuracy of the method applied.'

The first issue of the *Journal* was then published in February 1963, as volume 1 comprising six issues and a total number of 192 pages. This success was gratefully communicated to all those involved and, of course, used again to advertise this *Journal* and recruit new authors.

Looking back, though, there was also criticism. *Nepomuk Zöllner*, a co-worker of *Siegfried J. Thannhauser* (1885–1962) and member of the scientific advisory board of the *Journal*, said to *Joachim Brugsch* in January 1964 that he, as editor, had rejected three papers, and had accepted four others 'only after trimming and sharpening' them. In the case of two papers, he said, he had 'doubts about whether they actually belonged in the more narrow scope of the *Zeitschrift für Klinische Chemie*.'

In summary, he remarked:

'The articles I rejected, I rejected them partially because the papers did not contribute anything new, and partially because they had been carried out on the basis of poor methodology.

Perhaps you should make better use of your scientific advisory board. You do know that I am currently the Executive Editor of the *Zeitschrift für Experimentelle Medizin*, and I find it reassuring to have experts I can consult readily.'

Occasionally, the editors solicited external opinions on manuscripts, but manuscripts were not subjected to a regular peer review by two experts. Regular peer review was introduced only in 1971 (volume 9), as per the Acknowledgment at the end of each volume (e.g., volume 10, 1972).

Starting with issue 4 of volume 2 (1964), the *Journal* became the official journal of the German Society of Clinical Chemistry.

To commemorate the founders of the *Zeitschrift für Klinische Chemie*, *Joachim Brugsch* and *Ernst Schütte*, an additional line has been included in the first inner title page starting from issue 1, volume 24, 1986, but to my regret has been lost and forgotten 5 years later. After a short revival on the back of the first inner title page for 2 years, 1994/1995, they have been finally forgotten.

Hannes (Johannes) Büttner and the Clinical Chemistry

The curriculum vitae and the important role *Johannes Büttner* played in Clinical Chemistry could not be better formulated than by his friend *Dankwart Stamm* on the occasion of his 60th birthday [23].

Born on March 11, 1931, in Giessen, he studied Chemistry and Medicine and finished both with the doctorate. Already in 1956, he became head of the main hospital laboratory in Kiel.

'Through his fundamental scientific work, *Hannes Büttner* has played a decisive role in the development of Clinical Chemistry; his efforts on behalf of our discipline, and the high esteem and position of authority they have earned him, have brought attention and recognition to Clinical Chemistry both in Germany and abroad' [23].

Joahnnes Büttner was co-founder of the Deutsche Gesellschaft für Klinische Chemie in 1964 (see section 'The founding of the German Society of Clinical Chemistry (DGKC e.V.)' and [24]).

With the second reorganization of the *Journal* in 1971 (see section 'The further development of the *Journal*') *Johannes Büttner* became member of the Editorial Board of this *Journal*.

'As co-editor in 1971, as Editor-in-Chief since 1972, and as a contributor *Hannes Büttner* has had a lasting influence on this *Journal*. Through a happy combination of his various qualities, he has contributed very substantially to its recognition both nationally and internationally as a quality scientific journal and to its gaining an international readership' [23].

A further extensive dedication appeared on the occasion of *Johannes Büttner*'s 65th birthday, reflecting the history of our *Journal* and the important role *Johannes Büttner* played.

'In his decisions regarding, e.g., the development of the *Journal*, its scientific spectrum, its change to English as the preferred language, and its internationalisation, *Johannes Büttner* was consistent but careful and cautious, thoughtful and mindful, considerate and reflective. He had the skill and the good fortune to draw the right conclusions in every case at the right time. This is the reason for the success of his work for the *European Journal of Clinical Chemistry and Clinical Biochemistry*' (the *Journal*'s name at that time) [25].

The founding of the German Society of Clinical Chemistry (DGKC e.V.)

Ernst Schütte and *Johannes Büttner* reported: 'During the Mosbach Colloquium, April 24/26, 1964, *Werle*, in his capacity as the chairman of the 'Standing Committee', convened a meeting of clinical chemists. At that very lively meeting – ominous warnings originating from the Congress on Internal Medicine in Wiesbaden notwithstanding – the 'German Society of Clinical Chemistry' was founded thanks to the special efforts of *Günther Hillmann, Hansjürgen Staudinger* and *Otto Wieland* (1920–1998). At the first general meeting, *Werle* was elected Honorary President [14].

Günter Hillmann and *(Jo)Hannes Büttner* reported in a hidden note not listed in the table of contents on the founding of the German Society of Clinical Chemistry [24]: 'During this year's Mosbach Colloquium, the 'German Society of Clinical Chemistry (DGKC e.V.)' was founded on April 22, 1964. The head office of the Society is in Frankfurt am Main. The mission of the Society is the development and promotion of clinical chemistry at German universities and at the institutions of research, teaching and practical application. These include, in particular, clinical-chemical *research*, the training of *future specialists* in the discipline of clinical chemistry and the granting of *recognition* as a clinical chemist. The Society intends to establish close links to societies in neighboring countries. The Society's publication is the *Zeitschrift für Klinische Chemie*. The Board of the Society consists of the following gentlemen:

Prof. Dr. Ing. *G. Hillmann*, Nuremberg (Chairman)
Prof. Dr. med. *O. Wieland*, Munich (Deputy Chair)
Priv.-Doz. Dr. med. Dr. rer. nat. *H. Büttner*, Kiel (Secretary and Treasurer)
Prof. Dr. *H.J. Staudinger*, Giessen
Priv.-Doz. Dr. med. *D. Amelung*, Düsseldorf
Dr. med. *A. Oberdorfer*, Munich
Priv.-Doz. Dr. med. *H.-J. Dulce*, Berlin
Prof. Dr. med. Dr. rer. nat. *E. Schütte*, Berlin.'

Starting with issue 4 (1964), the *Zeitschrift für Klinische Chemie* became the official journal of the German Society of Clinical Chemistry (Table 1). The editors would have loved to continue printing such official 'communiqués', but negotiations failed. At the behest of *Helmut Schievelbein* and *Rosmarie Vogel*, both co-workers of *Eugen Werle*, the 'German Society of Clinical Chemistry Newsletter', issue 1, August 1969, was published. Editor of the Newsletter was *Helmut Schievelbein* (born 1949), and it was first published in 1969, after the 'Meeting of Biochemical Analysis' had been installed the year before

Year	Volume	Official Journal of
1964	2	German Society of Clinical Chemistry
1977	15	Austrian, German, and Swiss Societies of Clinical Chemistry
1981	19	Austrian, Dutch, German, and Swiss Societies of Clinical Chemistry
1986	24	Austrian, Belgian, Dutch, German, and Swiss Societies of Clinical Chemistry
1987	25	Austrian, Belgian, Dutch, German, Israeli, Luxembourgian, and Swiss Societies of Clinical Chemistry
1991	29	Journal of the Forum of Clinical Chemistry Societies (n=15)
1996	34	Journal of the Forum of Clinical Chemistry Societies (n=30)
1997	35	Journal of the Forum of Clinical Chemistry Societies (n=34) The European Branch of IFCC
1998	36	Journal of the Forum of Clinical Chemistry Societies (n=34) The European Branch of IFCC
1999	37	Published in association with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the Forum of the European Societies of Clinical Chemistry
2007	45	Published in association with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the Forum of the European Societies of Clinical Chemistry
2008	46	Published in association with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the European Federation of Clinical Chemistry and Laboratory Medicine (EFCC). *CCLM* is the official journal of the Clinical Chemistry Societies of Ireland (ACBI), Belgium (BVKC/SBCC), Germany (DGKL), Italy (SIBioC), and Slovenia (SZKK).
2009	47	Published in association with the IFCC and EFCC. *CCLM* is the official journal of the Clinical Chemistry Societies of Ireland (ACBI), Belgium (BVKC/SBCC), Germany (DGKL), Greece (GSCC-CB), Italy (SIBioC), and Slovenia (SZKK).
2010	48	Published in association with the IFCC and EFCC. *CCLM* is the official journal of the Clinical Chemistry Societies of Ireland (ACBI), Belgium (BVKC/SBCC), Germany (DGKL), Greece (GSCC-CB), Italy (SIBioC), Slovenia (SZKK), and Spain (SEQC).
2011	49	Published in association with the IFCC and EFCC. *CCLM* is the official journal of the Clinical Chemistry Societies of Ireland (ACBI), Belgium (BVKC/SBCC), Germany (DGKL), Italy (SIBioC), Slovenia (SZKK), and Spain (SEQC).
2012	50	Published in association with the IFCC and EFLM (formerly EFCC). CCLM is the official journal of the Clinical Chemistry Societies of Ireland (ACBI), Belgium (BVKC/SBCC), Germany (DGKL), Hungary (MLDT), Italy (SIBioC), Korea (KSCC), Slovenia (SZKK), Spain (SEQC), and Turkey (TBD).

Table 1 Globalization of the *Zeitschrift für Klinische Chemie* (1963) on to *Clinical Chemistry and Laboratory Medicine* (*CCLM*) (2012).

with the participation of *Schievelbein* and *Vogel*. Initially amateurish, the Newsletter 'grew up' and has been published now for 43 years as 'Clinical Chemistry Newsletter' with substantial scope and content.

How this *Journal* arose from the manuscripts

Authors – editors – reviewers – publisher/ editoral office – production – proof correction – make-up – imprimatur – printing – binding

The manuscripts submitted by authors were reviewed by the two Editors-in-Chief until 1970 for their suitability for publication, sometimes with the involvement of external experts, since 1971 with regular peer review by two external experts. On the editorial side, the manuscripts were checked by the Managing Editor and prepared (copy-editing) for typesetting. English texts written by non-native English speakers were reviewed and proofread by Dr. *Thomas A. Scott*, Leeds, UK, an employee at the Max Planck Institute of Biochemistry in Munich of many years and subsequent co-author of the 'Concise Encyclopaedia of Biochemistry' [26].

The *Journal* was typeset at the publishing house, on the basis of instructions given by the production editor. The typesetting was at first 'monotype', i.e., it consisted of individual letters that were cast and then stored in the type case. Such a type case still serves as a bric-à-brac wall decoration for the author. It has the shape of a drawer with 123 compartments of varying sizes for the individual letters – metal-cast types – each one representing a letter, character or number. Later this was replaced by 'linotype', entire lines cast as single elements. In case of necessary corrections, a gouge had to be used to remove letters from a monotype set to be replaced by letters from the type case. With the linotype method, the entire line had to be recast and replaced. The text was set as justified, i.e., with an even margin (unlike the 'ragged type'). For uniformity's sake, illustrations were prepared by a designer or drawn from scratch. In the printing plate facility, a printing plate, or cut block, was produced for relief printing.

Of the finished set, galley proofs were produced, that is, long sheets of paper without any page formatting, which were sent to the authors. The Managing Editor, too, acted as proofreader, verified that the requested and necessary corrections had been made, and again paid attention to whether the rules for writing manuscripts had been observed, particularly with respect to international recommendations on units, dimensions and nomenclature. Finally, the Editor-in-Chief would issue his imprimatur.

Following the corrections, the *metteur*, a specially qualified typesetter, finalized the form of the sheets of the issue, inserted illustrations and created the final page layout and format. Initially, this was done one article at a time. Subsequently, the galley proofs were produced with the proper page format, with each article being started on a new (left or right) page beginning with issue 6, volume 6 (1968). From volume 13 (1975), every article would start on a right-hand page, which substantially simplified the production of offprints.

Generally, printing presses were used for relief, flat and gravure printing. Good printing results require adjustment (levelling of the set). In the case of double-sided printing (recto and verso printing), the type areas have to overlap precisely when looked at against the light (register accuracy).

For the purposes of relief printing, used for this journal, raised elements in the printing form are coated with ink and printed on sheets on the printing press (one sheet=16 pages). Thus, the first volume consisted of 6×32 pages=6×2 sheets (Figure 1).

Later, composers made by IBM would be used to write in proportional font (the individual letters had different widths, e.g., i=2, m=5), i.e., the text was 'set' or typed on paper, often at home. By way of a photographic process, the type area was transferred to sheets of metal; the printing itself was done using flat printing.

In the beginning, a volume comprised six issues, then 12 issues starting with volume 10 (1972).

For the annual index, each keyword was written on an index card with the associated page number; each article was put on a separate card according to its primary author. Once the last issue of a year was completed, the information was alphabetized by hand, then set and printed. In the 1990s, the preparation of the annual index was facilitated with the advent of computers. Keywords, titles and author names were extracted from the articles but could now be arranged electronically.

With the advent of computers and information technology today, manuscripts are now prepared for typesetting and printing by the authors themselves and put to print through an online production system.

With a Publisher's Note [27] De Gruyter announced the introduction of the online submission and peer review system *Editorial Manager* from Aries in the middle of 2004.

'The *Editorial Manager* (EM) for *Clinical Chemistry and Laboratory Medicine* (*CCLM*) allows authors to upload files directly from their computer. Editors and Reviewers will access relevant files online, with most of

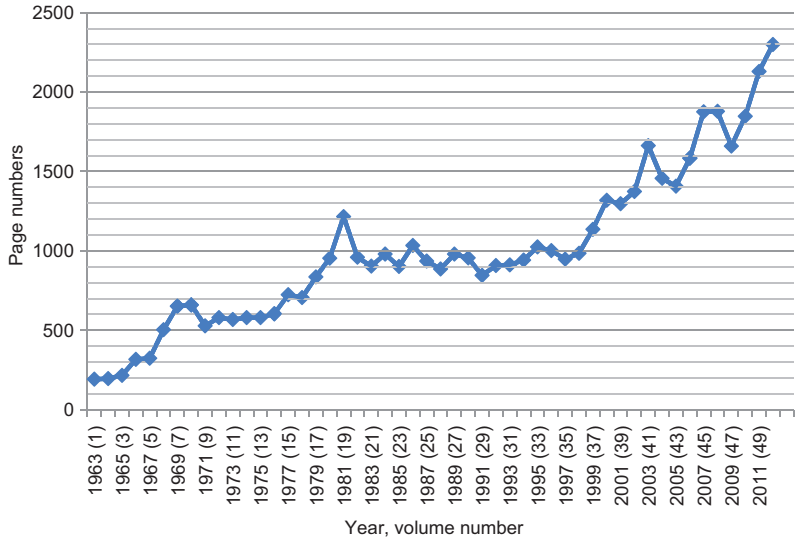

Figure 1 Number of published pages from 1963 to 2012.

the communication being done by e-mail. The system manages manuscripts from submission to final editorial decision, and authors will be able to track the status of their submission during the pre-production process.'

In early 2011, De Gruyter introduced its new online submission and peer review system, Thomson Reuter's *ScholarOne Manuscripts* together with *ScholarOne Production* [28].

'*ScholarOne Manuscripts* integrates manuscript invitation, submission, file conversion, correspondence, tracking, reviewer management, decision-making in one easy-to-use system. Proven author-friendliness of *S1M* fulfils the author's desire to submit quickly. The system manages manuscripts from submission to final editorial decision, and authors will be able to track the status of their submission during the pre-production process.

In addition, De Gruyter is also proud to introduce the new production workflow system *ScholarOne Production*. *ScholarOne Production* handles the copy-editing tasks, typesetting jobs, correction management, all within one system. Authors will receive their galley proofs directly from the system by e-mail notifications. *ScholarOne Production* offers an interface to the final editorial decision and manages manuscripts across the proof stage to the ahead of print publication and issue compilation.'

Distribution of the *Journal*, its content and the impact factor

The distribution of a journal is measured by the number of subscribers; the distribution of its content also by reference in collected editions or compilations, such as 'Current Contents'. The publishing house Walter de Gruyter had worked towards achieving inclusion of the *Zeitschrift für Klinische Chemie*. In this matter, *Ernst Schütte* wrote in early May 1964 to *Fritz Karl Beller* (1924–2008), a gynecologist at the New York Medical Center and member of the *Journal*'s scientific advisory board: 'A week ago, the publishing house received a curt rejection from Current Contents, along the lines of regretting it very much, but not considering in the least the possibility of referencing our little journal. A few days later an opposite message was received, saying that the Editorial Board had decided, following a letter you wrote, to include 'this excellent publication' in Current Contents. It could not be any clearer that we owe this success only to you.'

This illustrates also the importance of knowing the right people.

In his Editorial 'Thank you, indeed', *Mario Plebani* [29] explains: '....the IF is a measure, and as any measure, it carries inherent limitations, but no other measure has been found to be more effective to compare the value of scientific journals and, even more interestingly, to evaluate the behavior of each journal over time.' He announced 'that the recent release by Thomson Reuters of the 2010 impact factor (IF) showed a remarkable increase of our *Journal* impact factor (IF) to 2.069. *Clinical Chemistry and Laboratory Medicine*, for the first time since its foundation, has overcome the psychological boundary of 2.0. This is a milestone and we would like to build on it the future progress and developments for the journal and even more importantly, improvements of its usefulness and value for readers. ... the competition for available space improves

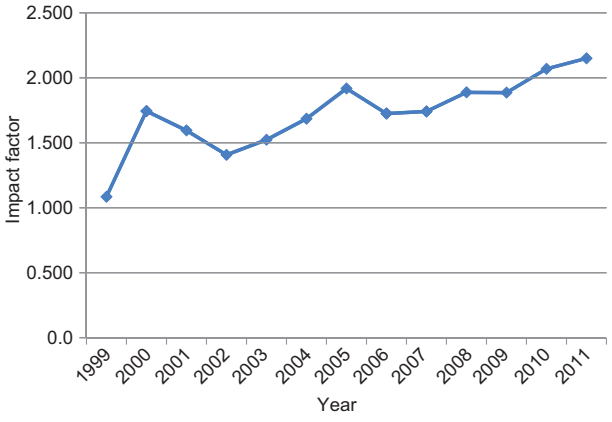

Figure 2 Development of *CCLM*'s Impact Factor.

the quality of published articles as substantiated by the significant increase in the rejection rate, which is now approximately 75%.'

The recent impact factor of *CCLM* (IF 2011) has even increased to 2.150 (see Figure 2).

Further development of the *Journal*

The first change to the *Journal* came with issue 1, volume 4 (1966): In addition to the names of the two Editors-in-Chief, the names of five co-editors were mentioned. In 1966 it thus read on the title page: 'With the participation of *Karl Bernhard, Heinz Breuer, Hans-Joachim Dulce* (new), *Hansjürgen Staudinger* and *Otto Wieland*.

Issue 4 of volume 4 (1966), comprising 100 pages (!), is titled '*On the Sixth International Congress of Clinical Chemistry in Munich, July 26–30, 1966*'. On the advertisement on page 27 between pages 176 and 177, one finds the '*Newsletter of the German Society of Clinical Chemistry*' indicated on the first cover page. *(Jo)Hannes Büttner* provides a brief report on the general meeting of the German Society of Clinical Chemistry in Mosbach/Baden on April 22, 1966.

Issue 6, volume 4 (1966), pp. 308–311 contains reports from the Sixth International Congress of Clinical Chemistry in Munich, July 26–30, 1966, with contributions by:

Klaus Borner (born 1936), *Klaus Krisch* (1928–1975), *Hans-Joachim Dulce* (born 1927), *(Jo)Hannes Büttner* (born 1931), and *Hermann Mattenheimer* (1921–2008).

With *H. Gerhard Schwick* (born 1928), *Ekkehard Kallee* (born 1922), *Axel Delbrück* (born 1925), *Otto Wetter* (born 1927), *Benno Hess* (1922–2002) et al., *Theodor Bücher* (1914–1997), *Wolfgang Pfleiderer* (born 1927), *Friedrich-Werner Schmidt* (1926–2007), *Feodor Lynen* (1911–1979), *Ulrich Matzander* (born 1922), *von Berg*, *Helmut Greiling* (1928– 2005), *Alfred Blume* (born 1945), *H. Werner Goedde* (born 1927), *Johannes Weis* (born 1937), and *Erich Gladtke* (1925–2002) as speakers – the active role by German representatives of clinical chemistry in the shaping of the congress is thus confirmed.

The *Zeitschrift für Klinische Chemie* did not only aim for the development, description and interpretation of chemical findings from the clinical laboratory, that is clinical chemistry, the term was coined in 1843 by *Johann Joseph von Scherer* (1814–1869) [30], but also for the biochemistry, this term was coined in 1877 by *Felix Hoppe-Seyler* (1825–1895), in healthy people and those who are ill.

Thus, the journal name *Zeitschrift für Klinische Chemie* was changed to *Zeitschrift für Klinische Chemie und Klinische Biochemie* beginning with volume 5 (1967) (see also Table 1 in [22]). Starting with issue 5 of this volume, Dr. med. *Friedrich Körber* took over as Managing Editor [31, 32], a position he remained in until issue 12, volume 35, 1997, that is, for a total of 30 years.

A second change to the *Journal* occurred with issue 1 of volume 9 (1971): The *Journal* was given a facelift and new people; seven members had already passed away, with only *Friedrich Hartmut Dost* (1910–1985), *Hans Faillard* (1924–2005) and *Jörg Frei* (?–2001) remaining. As co-editors joined: *Johannes Büttner, Günter Hillmann*, and *Dankwart Stamm*. New contributors were also brought on board: those active in clinical-experimental research, biochemists, statisticians, geneticists, endocrinologists and immunologists. They were to represent the *Journal*'s spectrum in future.

The further evolution of the *Journal*, in the wake of the rejuvenation at the start of volume 9, 1971, is reflected in the Editorials launched in 1977 (annually, beginning in 1985). These Editorials can be seen in Table 2.

The *Journal* was receiving an ever increasing recognition, both nationally and internationally, and as a result of that manuscript submission increased. Starting with volume 10 (1972), the *Journal* appeared in 12 issues. Given the increasing internationalization, the English title was added on the cover and title page (volume 10, issue 4). In 1976, the order of the titles was changed, with the English title now being the first title followed by the German one.

In the middle of 1977 (volume 15) the Austrian and the Swiss Clinical Chemistry Societies choose the *Journal* as their official journal, and further Societies followed the years after.

In 1989, the German title was discontinued and only the English title was kept, reflecting the growing number of contributions in English and the increasing internationalization of the *Journal*. Consequently, with volume 30 in

1992, the *Journal*'s name changed to *European Journal of Clinical Chemistry and Clinical Biochemistry*.

This era ended with the total renewal of the *Journal* in 1998 and its globalization, which was also reflected by the new name, *Clinical Chemistry and Laboratory Medicine* and the appointment of the new Editor-in-Chief, Prof. *Gérard Siest* (see section 'From 1998 to today and towards the future'). In early 2006, the Advisory Board, that had merely a political and no scientific function, was disestablished. In the same year, Associate Editors were appointed according to their fields of expertise, who, as from now, have processed manuscripts independently, beside the Editor-in-Chief.

The main messages of Editorials published in this *Journal* mirror this development (Table 2).

The development of life sciences in the 20th century and its influence on clinical chemistry

The founders of the *Zeitschrift für Klinische Chemie* realized soon after their appearance the importance of their maternal disciplines, Biochemistry and Chemistry as common roots. The title of the *Journal* has therefore already changed in its fifth volume to *Zeitschrift für Klinische Chemie und Klinische Biochemie* [22].

To the history of 50 years of *CCLM* belongs not only the development of the *Journal* itself but also the development of the scientific environment mirrored by its contents.

Three contributions describing a period corresponding to the age of the *Journal* impressed me. Therefore, I would like to mention them:

1. In his National Lecture '*Understanding Life as Chemistry*' presented at the Plenary Session of the Association of American Clinical Chemists National Meeting in Washington, DC, on July 28, 1991, *Arthur Kornberg* (1918–2007) stated: 'Although my investigations have taken several paths, my very earliest research was in clinical chemistry. ...In view of our current understanding .... I thought it would be appropriate on this occasion to talk about an issue of importance to us all: physicians, chemists, and lay people. It is a conviction that our appreciation of Nature and Life can be deeper and richer when expressed in the language of chemistry [33]'. He describes [33] the development of life sciences in the 20th century. You can read his contribution yourself in the original, because it is written in English. Therefore, I only give an overview.
2. *Herbert Keller* gives an overview [34] on the methodological development during 50 years of life as a clinical chemist. Essential parts are chosen and translated into English, therefore more extensively reviewed.
3. *Hansjürgen Staudinger* describes the development [35] regarding analytical aspects, quality and workload. He discusses the relationship between the laboratorian and the clinician.

Arthur Kornberg: Understanding life as chemistry [33]

In his national lecture *Arthur Kornberg* reflects on the history of medical science in the 20th century and describes five 'hunting' periods:

1. The microbe hunters tracking down the microbes responsible for, e.g., tuberculosis, cholera, diphtheria.
2. The vitamin hunters, dealing with diseases for which no microbe could be incriminated, e.g., scurvy, pellagra, rickets, beri-beri. Nutrition became a science, and it was discovered that these diseases were caused by the lack of trace substances in the diet.
3. The enzyme hunters, using the fact that some vitamins are essential as coenzymes, and therefore provide cells with energy for growth and function.
4. The gene hunters, discovering the importance of genes as matrices for enzyme synthesis. Defective genes are the cause of inborn errors of metabolism: diabetes, phenylketonuria, cystic fibrosis. Recombinant DNA technology becomes more and more important for the production of, e.g., hormones and vaccines.
5. The head hunters, applying the techniques of the enzyme and gene hunters to the functions of the brain. *Kornberg* is 'confident that the 'head hunters' who are now applying biotechnology to brain functions and diseases will soon be making startling advances in the understanding of sleep, memory, moods, mental illness, and other nervous system states' [33].

Recurring to the enzymes, *Kornberg* stated: 'Biochemists can saturate the enzyme with substrate, trap the product, and provide the optimal pH, salt and metal concentrations for the most incisive analysis of a reaction or pathway' [33]. This has been done also by clinical enzymologists, creating the Recommended Methods for diagnostically relevant enzymes, as published in this *Journal*.

Year	Volume (issue)	Page	Author(s)	Matter
1977	15 (6)	309	Delbrück A, Gabl F, Colombo JP, Büttner J, Schütte E, Körber F, Weber R.	Cooperation beyond international borders: Austria, Switzerland. New Editorial Board Members: *Hugo Aerbi*, Berne; *Erich Kaiser*, Vienna.
1981	19 (8)	513–4	Büttner J, Schütte E, van Dalen A, van Kampen EJ, Weber R.	Process of ever increasing cooperation: The Netherlands. New Editorial Board Member: *Esso Johannes van Kampen*, Groningen.
1985	23 (1)	1–2	Büttner J, Schütte E.	– Adaption to the rapid change due to progress in biochemistry, genetics, immunology, molecular biology. – New Board Members: *Walter G. Guder*, Munich (3rd Editor-in-Chief), *Joachim Kalden*, Erlangen. – Advisory Board: 13 new members.
		3–6	Keller H, Guder WG, Hansert E, Stamm D.	*Herbert Keller, Walter G. Guder, Erwin Hansert, Dankwart Stamm* describe and discuss the importance of: '*Biological influence factors and interference factors in clinical chemistry: general considerations*'.
	23 (8)	445	Büttner J, Guder WG, Haeckel R.	The Subcommittee of Instrument Testing of ECCLS proposes a standard protocol for the evaluation of newly developed analyzers ('Multicentre Evaluations')
1986	24 (1)	1–2	Büttner J, Guder WG.	Evolving international character of the *Journal*: – German title reduced in size; – The *Journal* becomes official journal of the Belgian Society of Clinical Chemistry; – New Editorial Board Member: *Vic Blaton*, Brugge. Advisory Board: 4 new members.
1987	25 (1)	1–3	Büttner J, Guder WG.	– Appearance of the 25th volume of the *Journal*. Starting in 1963 with a 192 page volume containing articles from the newly formed section of Clinical Chemists in Germany, the *Journal* has developed into an international organ of 7 National Societies (new: the Israeli and Luxembourgian Societies) representing 2500 members. – New Board Members: *Eitan Bogin*, Tel Aviv; *Herbert Keller*, St. Gallen. – Advisory Board: 6 new members for 2 years. Thanks to those Board members, whose term finished. – The German summary no longer seems necessary. – Authors are asked to submit camera-ready print figures in the future.
1988	26 (1)	1–2	Büttner J, Guder WG.	A short review of the history of the *Journal* is given. *Friedrich Körber* celebrates his 20th anniversary as Managing Editor of the *Journal*.
1989	27 (1)	1	Büttner J, Guder WG.	– *Hermann Mattenheimer* and *Esso Johannes van Kampen* (retirement) are replaced by *Norbert W. Tietz* and *Paul J. Brombacher* on the Editorial Board. – Advisory Board: 8 new members for the next 2 years. – *Nils-Erik Saris*, coordinator for IFCC Recommendations, is replaced by *John H.M. Souverijn*. – To promote internationalization, henceforth manuscripts can also be submitted to members of the Editorial Board. – From now on, references are to be published with the full article titles.
1990	28 (1)	1	Büttner J, Guder WG.	*Jörg Frei* (retirement) is replaced by *Walter Riesen* in the Editorial Board. Advisory Board: 6 new members
1991	29 (1)	1–2	Schönherr M, Büttner J.	– New title: *European Journal of Clinical Chemistry and Clinical Biochemistry*. – Hint to the scope of the *Journal* and the (Inter)National Editors. – Introduction of the membership subscription rate. – Sponsoring of subscriptions for institutions in Eastern Europe.
	29 (7)	457–8	Anonymous	25th anniversary of the German Society of Clinical Chemistry (DGKC): Preview: Clinical Chemistry in research, teaching and patient care, past and future.

(Table 2 continued)

Year	Volume (issue)	Page	Author(s)	Matter
		459–60	Wisser H.	Welcoming address of the DGKC President, *Hermann Wisser* (1933–2012). Hint to his personal request 'to concern ourselves with questions and problems beyond the day-to-day laboratory routine.' Therefore, he invited *Benno Müller-Hill* to give a lecture '*Science and Morals*' describing and discussing the involvement of the German doctors in the racial politics and crimes of the National Socialists (1933–1945).
		473–4	Körber F.	*Friedrich Körber* describes the statement and messages of *Benno Müller-Hill*, who repeatedly quoted the possible involvement of our former President (of the DGKC), *Günter Hillmann* (1919–1975) occupying the thoughts and feelings of the audience in a conflicting manner.
		461–70	Stamm D.	In his lecture 'Twenty-five years of Clinical Chemistry 1964–1989' *Dankwart Stamm* discusses challenges, progress and pitfalls.
1992	30 (1)	1–2	Schönherr M, Büttner J.	– 15 European IFCC Societies decided to support the *Journal* as journal of the 'Forum of European Clinical Chemistry Societies'. – An overview on the regional origin of the authorship is given: an increasing number of manuscripts come from countries others than Germany. – 60% of manuscripts submitted are finally published. Advisory Board: 3 new members.
1993	31 (1)	1	Noyer-Weidner M, Büttner J.	– The Croatian Society for Medical Biochemistry is added to the list of supporters of *the Journal*. – Advisory Board: 10 new members and renewals, respectively.
1994	32 (1)	1	Noyer-Weidner M, Büttner J.	– The Editorial Board redefines the form in which manuscripts have to be submitted for publication. Therefore, the 'Instructions to the Authors' are completely revised and considerably expanded. – All members of the Societies belonging to the 'Forum of the European Clinical Chemistry Societies' are granted a personal subscription rate for one copy of the *Journal* (DM 198.00). – The Slovak Society of Clinical Biochemistry and the Bulgarian Clinical Laboratory Society joined the 'Forum' and support the *Journal*. – Advisory Board: 7 new members and renewals, respectively.
	32 (8)	569	Noyer-Weidner M, Büttner J.	The new 'Instructions for Authors' (this J 1994;32:657–668) are extensively commented.
1995	33 (1)	1	Noyer-Weidner M, Büttner J.	– An overview on the regional origin of the authorship is given: increasing internationalization. – *Carlo Franzini* replaces *John H.M. Souverijn* as Coordinator for IFCC Recommendations. – Advisory Board: 13 new members and renewals, respectively.
1996	34 (1)	1	Noyer-Weidner M, Büttner J.	– Development of the *Journal* in 1995 is described (internationalization of the authorship, increase in manuscript submission, increase of printed pages, continuing cooperation with the IFCC). – Information about the *Journal* (Information to Authors, index, table of contents, subscription information) can be obtained online with immediate effect. – Advisory Board: 7 new members and renewals, respectively.
1997	35 (7)	485	Publisher's Note	With the publication of this issue, Professor *Gerard Siest* takes over as Editor-in-Chief for the European Journal of Clinical Chemistry and Clinical Biochemistry. He will share this office with Professor *Johannes Büttner* up until the end of the year, taking over sole responsibility as from the beginning of 1998. *Helmut Greiling* and *Erich Kaiser* leave the Editorial Board.

(Table 2 continued)

Year	Volume (issue)	Page	Author(s)	Matter
1997	35 (12)	891	Publisher's Note	*Johannes Büttner*, Editor-in-Chief, and *Friedrich Körber*, Managing Editor, retire at the end of this year. The publisher expresses their sincerest gratitude to both …. for their lasting commitment to the *Journal* and for their major contribution to the *Journal*'s success and its high international acceptance. The Boards are completely renewed, approximately one half of the members of the Editorial Board and Advisory Board are replaced by new members: *Bogin, Kalden, Lott, Férard, Kleesiek, Kostner, Van Lente, Mayer, Naskalski, North, Rossier, Thunell, Wagener, Wood*. We are grateful for their cooperation.
1998	36 (1)	1	Siest G.	Further globalization and internationalization takes place by omitting the restricting 'European' in the title and the entry of *Gérard Siest* as sole Editor-in-Chief. The new name of *the Journal* '*Clinical Chemistry and Laboratory Medicine*' (*CCLM*) reflects the reorientation of the *Journal*'s scientific scope. The aim is to open *CCLM* for an even broader international community of authors and readers, while maintaining the existing strong and fruitful relationship to the IFCC and FESCC (today EFLM).
2001	39 (1)	1	Siest G.	*CCLM* starts the new millennium with a great improvement in the quality of its papers. Thank you to all authors and reviewers! Increase of the publication of Letters announced. In future, *CCLM* will publish special issues. A special issue on reference values is announced.
	39 (2)	89	Whicher J.	To increase the quality of the articles published in *CCLM* 'reflected in higher scores in citation Indexes' and at the same time to give clinical chemists a 'reputable place to publish their own work where it will be read by other workers in the field together with a process of updating their relevant scientific knowledge'. *CCLM* will produce regularly special issues, containing original work along with reviews.
2002	40 (1)	1	Siest G.	Significant increase of the impact factor (1.74). Thank you to leaving Editorial Board members (*M. John Chapman, Gianni Messeri* and *Gerard T.B. Sanders*) and welcome of the new Editorial Board members (*Philippe Gillery, Johannes J.M.L. Hoffmann, Per Hyltoft Pedersen, Matthew McQueen and Mario Plebani*). Presentation of the further strategy: along with research articles, reviews, opinion papers, letters, historical papers, conference papers, thematic issues will be published.
2003	41 (6)	719	Siest G.	This issue contains articles on capillary electrophoresis. Announcement of special issues for 2003 (vitamins, diabetes and one on hyperhomocysteinemia), and for 2004 (on Reference Values; Call for Papers).
2004	42 (6)	575	Publisher's Note	Introduction of the online submission and peer review system *Editorial Manager* from Aries.
2006	44 (5)	513	Siest G.	'Significant organizational changes: '*Clinical Chemistry and Laboratory Medicine* (*CCLM*) has achieved the distinction of becoming one of the leading journals in the field of laboratory medicine. *CCLM* is now entering a new phase of development that will help further advance its international recognition and importance.'' – Introduction of the online submission and peer review system *Editorial Manager* (decrease of the time between submission, decision and publication of articles). – Appointment of Associate Editors (Reviews Editor: *Mario Plebani*; Editor for the Americas: *Steve Kazmierczak*; Editor for the Asian-Pacific Region: *Chris Lam*). – Increase in the number of the Editorial Board members (representing 'countries and regions from throughout the world. This helps ensure that expertise in all areas of clinical chemistry and laboratory medicine is represented.'). – Significant increase of manuscript submission and consequently increase of the rejection rate (55%).

(Table 2 continued)

Year	Volume (issue)	Page	Author(s)	Matter
2007	45 (1)	1	Kazmierczak S.	– '*Clinical Chemistry and Laboratory Medicine* (*CCLM*) is one of the leading journals in the field of laboratory medicine. Under the guidance of Chief Editor Professor *Gerard Siest*, the impact factor of this important journal has increased by 75% over the past 6 years; with an impact factor for 2005 of approximately 2.0. – *CCLM* has long been considered the premier journal for laboratory medicine within the European community. It currently serves as the official journal of the Belgian Society of Clinical Chemistry, the German United Society of Clinical Chemistry and Laboratory Medicine, and the Italian Society of Clinical Biochemistry and Clinical Molecular Biology. – More importantly, *CCLM* is the official journal of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the Forum of European Societies of Clinical Chemistry (FESCC). Working closely with these organizations, *CCLM* regularly publishes approved IFCC recommendations, and FESCC news.'
2008	46 (7)	883–4	Siest G, Plebani M.	– Evolution 'in the ever-changing scenario of medical laboratories thanks to the introduction of 'omics' into clinical practice'. – *CCLM* has always reflected and anticipated the changes in laboratory medicine (e.g., the name change 10 years ago). What is *CCLM* today and what should it be in the future? – One of the leading journals in the field of laboratory medicine (impact factor increased from 1.084 in 1999 to 1.725 in 2006; 'First and foremost, *CCLM* has to remain a tool for disseminating scientific information to laboratory professionals, and be a vehicle for making visible to a large audience the results of well-conducted research and scientific studies that result in reliable data useful for patient care'). – '*CCLM* is published in association with the IFCC, the European Federation of Clinical Chemistry and Laboratory Medicine (EFCC), and is the official journal of some national Scientific Societies in Europe.' – *CCLM* will attract more research papers in the fields of cardiovascular disease, cancer, neurological diseases, and aging. – Re-organization of the Board of Associate Editors. *Mario Plebani* (Italy) is Reviews Editor and responsible for the field of laboratory safety; *Steve Kazmierczak* (USA) is Letter Editor and responsible for outcome studies; *Ziyu Shen* (China) is responsible for the field of laboratory management and quality assurance; *Karl Lackner* (Germany) is responsible for the field of cardiovascular diseases. Search for two Associate Editors for cancer and neurology.
2009	47 (7)	791–2	Plebani M.	– July 1, 2009: *Gérard Siest* retires as Editor-in-Chief, *Mario Plebani* becomes new Editor-in-Chief; thank you to *Gérard Siest* for his extraordinary efforts and work for *CCLM* during 12 years as Editor-in-Chief ['The positive outcomes of the visionary changes promoted by Professor Siest are readily apparent: the extraordinary increase in the number of papers submitted for publication, the significant and consistent rise in the impact factor, the agreement with the IFCC and the European Federation of Clinical Chemistry and Laboratory Medicine (EFCC), as well as the decision of some national Clinical Chemistry and Laboratory Medicine Scientific Societies to settle on *CCLM* as their official journal.'] – 'Over the coming years …. *the Journal* will focus on cutting-edge research in technologies and clinical application of new biomarkers. However, first and foremost, it should continue to guarantee an updated and evidence-based source of information and knowledge.'

(Table 2 continued)

Year	Volume (issue)	Page	Author(s)	Matter
				– Since mid-2008, *CCLM*'s Associate Editors have taken over responsibility for a special field of expertise: in 2008: *Karl Lackner* (cardiovascular diseases), *Steven Kazmierczak* (quality control/ quality assurance and method evaluation); new in 2009: *Philippe Gillery* (metabolic diseases), *John B. Whitfield* (molecular diagnostics), and *Bohuslav Melichar* (cancer diagnostics).
2011	49 (1)	1	Publisher's Note	Change of the online submission and peer review system: introduction of Thomson Reuter's *ScholarOne* that provides new enhancements (plagiarism check, files can be attached to e-mails, author invitation through the system, resubmitted manuscripts become connected with the rejected manuscript).
	49 (11)	1759–60	Plebani M.	Significant increase of the impact factor, for the first time it 'has overcome the psychological 'boundary' of 2.0 (2.069)'. Thank you to all Associate Editors, the Editorial Board, reviewers and authors, and the IFCC and EFCC for their continuous support.
2013	51 (1)	1–2	Plebani M.	Happy 50th anniversary! Name change of the *Journal* in accordance with the development of the profession of laboratory medicine; description of the development and recognition of the profession. 'Navigating many obstacles, *CCLM* needs to continue adapting to a changing environment, improve its ability to guarantee the quality of the peer-review process, maintain transparency in decisions regarding the rejection/acceptance of any paper, and ensure the integrity of publications and avoid the risk of plagiarism and fraud. These tasks require the effort and cooperation of many stakeholders. Therefore, the celebration of the 50th anniversary is an opportunity to thank all Associate Editors, members of the Editorial Board, the huge number of valuable referees who have agreed to review manuscripts and are willing to spend the time evaluating the quality of submitted papers, and last but not least, our authors and readers. I truly hope that *CCLM* may continue to be a valuable source of knowledge and information for laboratory professionals first, but also for physicians and scientists around the world. Happy 50th anniversary!!'
2013	51 (1)	5–7	*CCLM* Associate Editors	50 years of *CCLM* 'offer a formidable opportunity to look back for moving forward'. – Increasing popularity of the *Journal* after the name change in 1998. – 1998: setup of the *CCLM* website. – 2004: introduction of the online submission and peer review system. – As of 2013: Letters and Congress Abstracts will be published online only. – Scientific impact to improve 'the practice of our subject and therefore improve healthcare'. – Scientific impact is reflected by the number of citations and the increased impact factor. – Official journal of IFCC and EFLM. – Description of the means with which *CCLM* protects against plagiarism and unethical behavior. 'Navigating many obstacles, *CCLM* should adapt to changing environments in order to safeguard its mission that is to provide reliable information and updates to our readers. This is the only way to celebrate in the future the 100th anniversary.'

Table 2 Messages from Editorials as regards the development and policy of the *Journal*, published 1977–2013.

Herbert Keller: 50 years clinical chemistry, as lived

In his article, '*50 years clinical chemistry, as lived*' (1945–1995), *Herbert Keller* (1925–2001), Editorial Board member of this *Journal*, delivered a chronological overview in nine chapters of this discipline in relation to methods and procedures [34].

1. Photometry

Here, *Keller* writes about a previous encounter with *Hans Ulrich Bergmeyer* (1920–1999) at the Chemistry Department of the University of Bonn, and there, with a photometer. He describes the efforts of *Theodor Bücher* (1914–1997), together with Dr. *Heinrich Netheler* (1909–1999), Hamburg-Eppendorf, in developing the measurement principle used by *Otto Warburg* (1883–1970) into a useful routine device.

2. Industrially manufactured reagents

In 1954, *Hans Ulrich Bergmeyer* became the director of the Tutzing laboratory of Boehringer Mannheim, which he continued to head until 1985.

He threw himself into the production of biochemical reagents. Within an astonishingly short amount of time, as early as 1955, it was possible to buy DPN and TPN (today: NAD and NADP), ATP, ADP and a number of enzyme preparations. At the International Congress of Biochemistry in Brussels, 1956, *Bergmeyer* presented the first test combination for enzyme analyses. The reagents and associated watery solutions were readily quantified and packaged; the user merely had to mix them together – weighing and precise volumetry were no longer necessary. Given the relatively high prices, many predicted his test combinations would turn into a fiasco, but the sceptics were wrong: the future proved him right.

Under his leadership, Tutzing became not only the most important production center for biochemical reagents in the world, but it also evolved into an internationally highly respected scientific center of enzymology, as demonstrated by a large number of publications and an encyclopedic standard tome [36].

The commercial availability of biochemical reagents for clinical chemistry was characterized by *Walter Guder* (born 1938) '... as a key turning point in the development of our discipline ...' [37].

3. Automation, part I

Despite this substantial facilitation for analytical work, clinical laboratories experienced ever more growing bottlenecks in terms of staff and space: the number of research contracts grew exponentially, and the number of analyses doubled every 4 years. There was only one solution: automation. It started with the 'Autoanalyser': *Edwin C. Whitehead* (1919–1992), the son of the company founder of Technicon, *Edwin Weisskopf* (1892–1968), writes in his 'History of Technicon Corporation' [38]: '... in 1954, at a time when Technicon was still a relatively small company that turned over around 2 million dollars a year, Dr. *Leonard Skeggs* (1918–2002) approached us with an idea of how an automaton should be designed that could carry out clinical-chemical analyses automatically ...'

The essential and highly original design principle is the 'continuous flow' that is interrupted by air bubbles intermittently.

The Autoanalyser built by Technicon in New York was thus the first reliable, functioning, industrially manufactured analysis automaton. The first publication to describe the system came out in 1957 [39].

In the following 25 years, this principle was used to develop newer, faster and more powerful types and modules for different applications, including hematological test methods. However one day, the limits of this analysis principle had been reached: without *Skeggs* and *Whitehead*, the imitators had taken the continuous flow principle in a wrong direction. Almost instantly autoanalyzers lost their market lead, to be replaced by machines from Japan that were far from being original but much more powerful.

4. Microliter techniques

Regardless of the so-called analysis automation, there were, and still are, analytical procedures that have to be done manually. In this context, a new aspect emerged with the arrival of microliter techniques, which had been developed independently and separately at various locations, including Eppendorf.

In his company's history, Dr. *Netheler* writes [40]: '...Dr. *Bücher* had meanwhile become a full professor of physiological chemistry at the University of Marburg (1953)... He informed us occasionally that his colleague Dr. *Heinrich Schnitger* had developed a new pipetting technique for small volumes... He was especially interested in volumes in the range of 1–10 µL... We agreed with Dr. *Schnitger* on an adjustment of this technique for the requirements of clinical chemistry (10–500 µL)...' Almost at the same time, similar microliter systems had been developed by *Sanz* [41] in Geneva and *Mattenheimer* [42] in Berlin. However, the Eppendorf system became more widely used and was soon copied by many competitors.

An article on the subject was published in 1974 and originated at the laboratory in St. Gallen: in a conversation with Dr. *Gerken* from Eppendorf, the possibility was discussed to expand a Marburg pipette in a way that would allow for multiple dispensing. This resulted not only in a

small sketch but also in the name 'multi-pipette'. A year later the multi-pipette arrived on the market and became one of the most successful products of the company Eppendorf.

5. Immunoassays, part I

Perhaps the most consequential development in those exciting 1950s, however, came about in an entirely different field: radioimmunoassays opened new analytical dimensions.

Keller describes the history of the development of radioimmunoassays by *Rosalyn S. Yalow* (1921–2011) and *Salomon Berson* (1918–1972) up to the time when their manuscript was rejected by *Science* and the *Journal of Clinical Investigation*.

Before describing the further development of immunoassays, one must first, due to the chronological sequence, describe the progress achieved with respect to electro-mechanical analyzers:

6. Automation, part II

Here, *Keller* refers to the Dupont ACA, a prototype of a 'closed system', and reports on the concept of the centrifugal analyzer by *Norman G. Anderson*, Analytica laureate 1972 [43, 44].

In addition, one must refer to *Roland Richterich* (1927–1973) at this point, who developed his analytical principle with *Rudolf Greiner* (1909–2006) and *Hans Küffer* (born 1940) and published it in this *Journal* [45–51].

7. Immunoassays, part II

Radioactive isotopes come with substantial disadvantages for analytical purposes: their production, shipping, storage and disposal are complicated and more expensive; radiolytic processes can change immunological properties, the metering devices are complex, and regulatory restrictions tend to be an annoyance – many reasons for looking for non-radioactive tracers. In the case of heterogeneous enzyme immunoassays (EIA), radioactive tracers are replaced by enzyme-labeled ones.

The preferred procedure was to immobilize the primary antibody, which binds the analyte primarily, on the wall of plastic tubes (or on plastic balls). All subsequent separation and washing steps can then be carried out much more easily (for an overview, see [52]).

The measuring instrument is a simple photometer. Generally, this paved the way for immunoassays to be done also by medical assistants at the practice laboratory, which soon became a reality. Consequently, a very large number of modifications to the principle of heterogeneous EIAs were described: Kodak developed several assays based on the 'dry-chemical' Ektachem principle (Review by *Wisser* et al. [53]).

At this point, one should also mention the Europium-based Delfia system, the Stratus and luminescence immunoassays.

'All heterogeneous assays, invariably require manual or mechanical intervention with individual process stages, for example, to move tubes or microplates to washing stations, dispenser units or a measuring system. This is why the corresponding analysers are either semi-mechanical or rather complex in design.

A substantial simplification was triggered by 'homogeneous' immunoassays, which made possible continuous mechanisation, that is, an automatic process sequence from entering the specimen material to printing out the results.'

From the variety of procedures, let us look at only one (FPIA) in greater detail.

Dandliker [54] developed the fluorescence polarization immunoassay at the laboratories of the Scripps Clinic in La Jolla, also in the early 1970s: if a fluorescent molecule is activated by polarized light, fluorescence polarization occurs. The orientation of the fluorescence ray matches the orientation of the activation ray only if the fluorophore, e.g., is fixed to a macro molecule, such as an antigen-antibody complex. If a fluorescent hapten (e.g., a drug) rotates freely in the solution, no directed polarization occurs. However, if it is fixed by means of a specific antibody, the secondary ray is polarized, and is the stronger, the more labeled hapten molecules are fixed by antibodies. This elegant procedure was published in 1973 (without registering a patent), and no one showed any significant interest in it – until 8 years later, in 1981, when the company Abbott presented the TDx, a system based on it, and thus became the market leader in hapten immunoassays.

8. Monoclonal antibodies

A scientific sensation was the development of the techniques for obtaining monoclonal antibodies by *Köhler* and *Milstein* in 1975 (Analytica Prize 1982) [55, 56]. Monoclonal antibodies have a high specificity, and – frequently even more importantly – there is an unlimited supply of them while keeping the quality constant. Naturally, monoclonal antibodies are often of great value with respect to the reliability of analytical procedures, because they permanently – i.e., regardless of the batch – exhibit the same properties. But this is also a special advantage for producers. 'Monoclonal' is not a seal of quality *per se* that should justify a purchase, however. In reality, the affinity of polyclonal antibodies to the antigen may be greater in individual cases, and left unmodified, there is no substitute for polyclonal antibodies when it comes to specific analytical problems.

9. Polymerase chain reaction

At the end of this chronology, naturally, we find genetic technology and the polymerase chain reaction (PCR). The polymerase chain reaction – and analogous procedures – will change, one can say with certainty, the laboratories of many disciplines drastically in the near future. Practical applications for analytical problems have so far been encountered mostly in the areas of microbiology and virology. Applications in the field of cellular diagnostics, such as the identification and classification of malignant changes, have been established in research laboratories, and their practical implementation may not be that far off anymore.

Like the development of RIAs, the concept of the PCR was also ahead of its time. When *Mullis* sent in the manuscript describing this epochal discovery to *Nature* in 1985, it was returned to him immediately with the note that '...this paper is at best suited for a specialised journal ...'. The attempt to get it published in *Science* also failed. The peers wrote to him matter-of-factly: 'The paper could not compete with our limited space...' [57, 58].

The authors of the polymerase chain reaction, *Kary B. Mullis* (born 1944) and *Henry A. Erlich* (born 1943) received the Analytica-Prize 1990 [58] and *Kary B. Mullis* the Nobel Prize in Chemistry 1993.

Hansjürgen Staudinger: Look back and outlook 1985 – two decades after founding of the *Journal*

In his closing words on the occasion of the Mannheim laboratory anniversary in 1985 [35], the chemist *Hansjürgen Staudinger*, Director of the primary laboratory of the Municipal Hospitals in Mannheim from 1948 until his appointment to the Chair of Physiological Chemistry at the University of Giessen in 1959, and Editorial Board member of this *Journal* from its beginning to 1986, wrote: 'With a few selected considerations on the history and future of clinical chemistry, I wish to conclude this book on the 75th anniversary of the central laboratory of the Municipal Hospitals of Mannheim. My reflections are grounded in the circumstance that I headed up this central laboratory at a time that saw the start of a qualitatively new stage in the evolution of clinical chemistry. On earlier occasions, too, I have tried to take stock critically of the interdependence between medicine and biochemistry.

Until around 1960, hormone research did, relatively speaking, what immunology does today. However, at the same time, first only gradually, but then with increasing speed, actual clinical chemistry evolved and emerged, which I also like to call 'analytical chemistry in a clinical setting'. The progress achieved in the last three decades is essentially based on an ongoing improvement in the following four areas:

1. Improved sensitivity

This refers, e.g., to the use of small amounts of test material (e.g., blood, which is important in pediatrics), but it also refers, e.g., in endocrinology or toxicology, to the possibility of determining substances that occur in body fluids in only very small amounts. A key requirement for this development were improvements in the area of analytical instruments.

2. Improved specificity

The methods used in the clinical-chemical laboratory are to determine, where possible, only the one substance targeted without disturbing other, similar, substances. The crucial breakthrough in this area was accomplished with the introduction of enzymatic analysis.

3. Improved analytical reliability

In this area, the introduction of 'statistical quality control' in the mid-1960s proved to be a blessing. The comparability of results from all areas of clinical chemistry can today be proved by the findings of round-robin testing.

4. Reduction of work input

I am always astonished by how little today's young researchers in biochemical and analytical laboratories are aware of the fact that the tools they use – the various devices and automatons they use every day and that, seemingly with hardly any effort, provide them with a variety of measured data – have been a fairly recent development. After all, who thinks about the fact that progress in science reflects the progress in methodological possibilities, particularly as concerns the equipment used?

Technology today manifests itself in clinical-chemical laboratories as an ensemble of machines and devices whose functions we of the older generation, going back to the beginnings of clinical chemistry, have a hard time understanding.

How quickly clinical chemistry analysis has advanced is plain to see in a development I was involved in during my Mannheim days. When I took over as director of the central laboratory in 1948, there was no photometer yet – although there was a Pulfrich photometer, whose principle was based on the visual comparison of one light intensity to a reference light intensity. As for quantitative work, there were generally only three methods available to me: the analytical balance (highly sensitive and accurate), volumetric measurement by means of a pipette and burette, and a small device, by now a museum piece, for

colorimetric analysis – the 'Duboscq Colorimeter', named after its inventor, that made it possible to estimate and compare two color intensities. While the balance and burette allowed for precise and sensitive, albeit time-consuming, measurements, the colorimeter was not as accurate, but useful for quick measurements.

Analysis of the glucose content of whole blood according to the method of *Hagedorn* and *Jensen* (who still remembers those names?) was surprisingly sensitive for analytical chemistry as it was then. With this method, it was possible to determine 2×10^{-7} mol glucose in 0.1 mL of whole blood. An experienced laboratory technician or technical assistant was able to run 20–25 double analyses according to *Hagedorn-Jensen* a day. Today's automated equipment – if there is any limit at all – can easily accomplish a hundred times more.

Between the time when blood sugar was measured titrimetrically and today, 1985, there is one phase in which I helped to shape myself. The photoelectric photometer, which measures extinctions of solutions at specific wavelengths, was then a revolutionary innovation in analytical chemistry in general, and especially in clinical chemistry. This was followed by the introduction of optical tests according to *Otto Warburg* as routine methods. Both the introduction of an easy-to-handle photometer and the development of optical test methods for the clinical-chemical laboratory were in large part the work of *Theodor Bücher* (1914–1997). People should remember that!

Similarly, one must mention the contributions of industry, not to be underestimated, which played a substantial part in this development. On the one hand, there was the company *Netheler* and *Hinz* that developed the handy Eppendorf photometer with *Bücher*. On the other hand, the company Boehringer Mannheim, at its plant in Tutzing and headed by *Hans-Ulrich Bergmeyer*, started the manufacture and sale of biochemical reagents, both coenzymes like NAD or ATP and enzymes like alcohol: NAD^+ oxidoreductase (EC 1.1.1.1), ADH, or (S)-lactate: NAD^+ oxidoreductase (EC 1.1.1.27), LDH, which had to be prepared painstakingly in each laboratory.

This reflection shows examples of the fast development of methods in biochemistry, and in particular, in clinical chemistry. Many new methods to analyze different substances, metabolic products and enzyme activities have tremendously increased the number of diagnostic options available to doctors.

When I began building the clinical-chemical laboratory in Mannheim after the war, the routine diagnosis of liver conditions was limited to determining the direct and indirect bilirubin and testing for serum lability, such as 'Takata-Ara' or 'Mancke-Sommer'. Since then, there has been such an abundance of new biochemical indicators to assist doctors in the differential diagnosis of liver diseases and assessment of the severity of the condition.

When we look at all this, the increase in methods and the acceleration in carrying them out, then it is not surprising that the number of tests per patient, but also per laboratory employee, has increased dramatically. The statistical data collected at the Mannheim clinic over the last 30 years from 1950 to 1980 can be seen in the following Table 3 according to *Kattermann* [59].

While two clinical-chemical tests were performed for each patient in 1950, the number has gone up to almost 50 by 1980, i.e., one generation later – an increase by a factor of 25! There is no denying that the increase and improvement of the methods available have expanded the diagnostic possibilities of doctors enormously. However, one can also ask critically whether a doctor can still process such a deluge of data for each patient in any meaningful manner.

Perhaps, something else also bears mentioning in this context. Given the painstaking nature of many chemical analyses in the early days of clinical-analytical chemistry described, there was frequent intense conflict between the laboratory head – who could not expand the capacity of his laboratory, where analyses were still

Year	No. of tests	Staff members	No. of tests per staff member	No. of patients	No. of tests per patients	No. of nursing days	No. of tests per nursing days
1950	43,069	8	5,400	21,000	2.0	521,000	0.10
1955	96,238	11	8,700	25,647	3.7	605,550	0.16
1960	157,319	15	10,500	26,706	5.9	592,357	0.26
1965	203,051	25	8,100	29,104	7.0	586,263	0.35
1970	599,220	36	16,600	31,536	19.0	586,864	1.02
1975	1,118,071	46	24,300	37,105	30.1	558,206	2.00
1980	2,017,833	48	42,000	42,126	47.9	532,858	3.80

Table 3 Efficiency of the Clinical Chemical Institute in relation to the number of staff members and nursing days, shown for the years 1950–1980. Note the remarkable effect of rationalization in the laboratory between the years 1975 and 1980.

done 'manually', as he saw fit – and the physician who needed the analysis done to clarify a diagnosis or monitor the treatment, which created tension at times. The physician would reject the verdict of the analyst concerning the necessity of a test ordered. At the same time, the analyst was often able to prove the lack of consideration and insight that went into the ordering of chemical tests. He had to do so quite frequently to prevent his laboratory and staff from being exposed to excessive demands, which could have jeopardized due care. This environment of tension was very healthy for both, the doctor and the laboratory head. The doctor was forced to consider his diagnosis carefully. The laboratory head, a chemist or a medical doctor, was motivated to talk with the doctor, at the patient's bedside, about his predicament, his doubts about the diagnosis or the accuracy of a chemical analysis.

Obviously today, a laboratory can hardly be overwhelmed anymore by the number of tests ordered. It is therefore more economical to run all sorts of analyses, even unnecessary ones, through an automatic analysis device than having to go back to the physician who ordered the test to be reassured about the diagnosis and usefulness of the test. This leads, I suspect, to alienation between the clinic and its doctors, and the laboratory and its staff. The latter deliver the analysis results blindly as a 'service', while the former merely juggle numbers at the bedside, the pathophysiological significance of which they often fail to appreciate correctly. 'Normal' and 'abnormal' readings are, for the recipient of data, often separated only by an imaginary line that has little to do with the reality of the normal distribution of normal and pathological results. These sceptical remarks, incidentally, do not only apply to the alienation between doctors and the clinical-chemical laboratory, but also, quite generally, to the many diagnostic specialist departments of a clinic where a high level of specialized expertise is a requirement for high performance.

The future and perspectives of clinical chemistry

In closing, I should like to quote some observations made by *Arthur Kornberg* [33]: 'Whether it be diet or behavior, health or disease, much of life and medicine can ultimately be understood in rational terms if expressed in the language of chemistry. Chemical language has great esthetic beauty and links the physical sciences to the biological sciences. It is an international language without dialects. It is a language that explains where we came from, what we are, and where the physical world will allow us to go.

The influence of our expanding knowledge of body chemistry has already been large, but in the coming years the impact will be astronomical. We will have identified the thousands of genes that encode the precise chemistry of each cell and tissue. We will know each of the many thousands of enzymes, the hormones, cytokines, and neurotrophins. We will be able to measure the amounts of their building blocks and of the metal ions, salts, and vitamin coenzymes essential for the assembly of the macromolecular proteins, lipids, and carbohydrates.

Who will determine the encyclopedic 'geneprint' and 'chemprint' of each patient needed to provide the correct diagnosis of an aberration and to select the proper regimen for prevention and treatment of disease? Who will determine from these geneprints and chemprints the optimal dosage of the proper drug and then monitor its efficacy and untoward side effects? The patient and physician will need and demand these data. I expect that most clinical chemists will assume a considerable share of this staggering responsibility. If they should not, then some other disciplines will have to emerge to shoulder this daunting assignment.'

The *Journal* was completely changed in 1997/1998; De Gruyter publishers announced in their Publisher's note entitled '*To our Readers, Authors and Subscribers*' in the December issue of 1997: 'This issue marks an important step in our *Journal*'s development as it will undergo major changes from the beginning of next year. Importantly, the *Journal*'s title will change to *Clinical Chemistry and Laboratory Medicine*' (*CCLM*) reflecting reorientation of the *Journal*'s scientific scope. …. The aim of these changes is to open the *Journal* to an even broader international community of authors and readers while maintaining the existing strong and fruitful relationship to the IFCC and FESCC. ….. We would like to take this opportunity to express our sincerest gratitude to Professor *Johannes Büttner*, Editor-in-Chief, and Professor *Friedrich Körber*, Managing Editor, who retire at the end of this year, for their lasting commitment to the *Journal* and for their major contributions to the *Journal*'s success and its high international acceptance. We would also like to cordially thank the new Editor-in-Chief, Professor *Gérard Siest*, for taking responsibility for the *Journal*'s future. We will give both him and the members of the Editorial Board our fullest support in making the planned changes a success' [60].

From 1998 to today and towards the future

In 1998, *Gerard Siest* introduced a seminal change in the *Journal*'s life by renaming it as '*Clinical Chemistry and Laboratory Medicine*' (*CCLM*). The change reflected two main goals. First, by understanding the increasing importance of globalization and internationalization processes, *CCLM* became the official Journal of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and thereafter, of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM, formerly EFCC). The latter resulted from the merger of two well-known European entities, the Forum of European Societies of Clinical Chemistry (FESSC) and the European Communities Confederation of Clinical Chemistry and Laboratory Medicine (EC4). One of the major duties of *CCLM* was and noticeably remains the publication of 'official papers' of both Federations – recommendations, practice guidelines, surveys, standardization and harmonization initiatives.

Second, the new name better reflects the reorientation of the scientific scope of the Journal that, preserving the historical background in clinical chemistry and biochemistry, would now embrace topics such as molecular biology, hematology, hemostasis and microbiology. As such, *CCLM* will remain 'the' journal for laboratory professionals, acknowledging and promoting the evolution of clinical laboratories. Indeed, the changing face of clinical laboratories was reflected in the title of an opinion paper published in 1999, which provided evidence of the changes and designed the evolution of the discipline [61]. In 2001, another important step was the decision to publish special issues dedicated to relevant topics in laboratory diagnostics (Table 2). Special issues, e.g., on pharmacogenetics, clinical proteomics and vitamins, and more recently on patient safety, cancer research and reference ranges, have been highly appreciated by the scientific community.

In 2006, *Gerard Siest* appointed *Mario Plebani* as a Reviews Editor, recognizing the importance of this type of scientific publication. The value of reviews cannot be merely regarded as an important source of citations and thus as a useful tool for improving the Impact Factor (IF). The main value of reviews is, in fact, to provide the readers with an easy-to-use tool for updating their knowledge and being informed of state-of-the-art in relevant scientific topics.

In 2004, De Gruyter publishers introduced the online submission and peer-review system *Editorial Manager* issued by Aries. By use of this system, manuscript submission became easier and peer review faster and more transparent. In fact, the time between submission, decision and publication of articles dropped down significantly.

In 2006, *Gerard Siest* promoted another significant organizational change by appointing *Steve Kazmierczak* as an Editor for the Americas and *Chris Lam* for the Asian-Pacific Region. The fact that China currently takes first place among contributing nations, and the American countries occupy a relevant position in rank, is mainly due to the valuable job done by those scientists, and by the other members of the Editorial Board. In 2008, an Editorial written by *Siest* and *Plebani* recognized the changes in the discipline due to the explosion of the 'omics' and underlined the willingness (commitment) of the *Journal* to publish papers related to this issue to remain a tool for disseminating scientific information to laboratory professionals, as well as to be a vehicle for a wider audience [62]. This aspect has been also underlined in an article published by *Plebani* and *Marincola* in 2006 [63] that emphasized the importance of research translation as a new deal for clinical laboratories.

In the middle of 2008, after the retirement of *Gerard Siest* as Editor-in-Chief, *Mario Plebani* was appointed as new Editor-in-Chief of *CCLM*. In 2010, the *Journal*'s cover and format were changed. The introduction of a new online submission and peer review system in 2011, i.e., Thompson Reuter's *ScholarOne*, has improved the quality of editorial processing, as it provides a tool for plagiarism check. Plagiarism, as well as other unethical habits in scientific writing, such as duplicated, flawed or even false research, represent an ever increasing problem and threat for editorial activities, and electronic support is an invaluable tool for detection. However, first and foremost, the new organizational editorial structure, i.e., the appointment of six Associate Editors according to special fields (2008/2009), allows a more active and joint decision-making process. As a result of all these initiatives *CCLM*'s Impact Factor has overcome the boundary of 2.0 for the first time since its existence, being 2.069 in 2011 and finally 2.150 in 2012. The 2.0 cut-off does not only represent a 'psychological barrier' for readers and potential authors, but it is also a 'hallmark of excellence'. From a scientific standpoint, in fact, 67% of existing journals fall into the category termed 'below 2.0', while the journals that exceed this threshold are competing and striving for excellence.

The 50th anniversary celebration is a unique opportunity to recognize the efforts of so many scientists who played the role of Editor-in-Chief, Associate Editors, members of the Editorial Board, referees, authors, and of course of the publisher. I hope that everyone that had and

still have a crucial role in the *Journal*'s history have been recognized in this article, but I should apologize for any eventual hole and/or omission.

Conclusions

In an Editorial published in November 2011, *Mario Plebani* [29] says: 'In 2012, *Clinical Chemistry and Laboratory Medicine* celebrates its 50th anniversary. We would like to take this opportunity to 'look back for moving forward', and therefore, we are inviting readers and laboratory professionals to submit proposals and ideas to celebrate this event in a memorable way'.

In the sense of this 'look back' we hope that our look at the history of *CCLM* and Clinical Chemistry and Laboratory Medicine as a profession will find the interest of the *Journal*'s readers and shows the tremendous and exciting development that *CCLM* has been making since its foundation 50 years ago.

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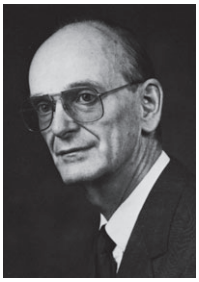
References

1. Stamm D. Die Gründung der Deutschen Gesellschaft für Klinische Chemie. J Clin Chem Clin Biochem 1978;16:484–9.
2. Berlin-Krise. Available from: http://de.wikipedia.org/wiki/Berlin-Krise. Accessed June 2012. See also: Wettig G. Chruschtschows Berlin-Krise 1958–1963. Drohpolitik und Mauerbau. München 2006.
3. Watson CJ. On acute intermittent porphyria. Z Klin Chem 1964;2:25–8.
4. Ziesak AK. Der Verlag Walter de Gruyter 1749–1999 mit Beiträgen von Hans-Robert Cram, Kurt-Georg Cram und Andreas Therwey, X+292 pp., Berlin, New York: Walter de Gruyter, 1999:263–4.
5. Strehl H. Zum Tode von Professor Dr. Joachim Brugsch. Die Berliner Ärztekammer 1981;18:19.
6. Stürzbecher M. Joachim Brugsch (1909–1980) – Der "Porphyrin-Brugsch". Hainblick 2000;10:2–4. (Hauszeitschrift des Krankenhauses am Friedrichshain in Berlin).
7. Dulce HJ. Ernst Schütte zum 60. Geburtstag. Z Klin Chem Klin Biochem 1968;6:227–8.
8. Büttner J. Ernst Schütte 65 Jahre. Z Klin Chem Klin Biochem 1973;11:223.
9. Delbrück A. Ernst Schütte 70 Jahre. J Clin Chem Clin Biochem 1978;16:321.
10. Körber F. Verleihung der Scherer-Medaille an Ernst Schütte. J Clin Chem Clin Biochem 1978;16:473–91.
11. Büttner J. In memoriam Ernst Schütte. J Clin Chem Clin Biochem 1985;23:321–2.
12. Körber F. Prof. Schütte verstorben. FU-INFO 1985;8:20.
13. Siegmund P, Schütte E, Körber F. Praktikum der Physiologischen Chemie, 1st ed. Berlin: Walter de Gruyter, 1968.
14. Schütte E, Büttner J. Eugen Werle und die Deutsche Gesellschaft für Klinische Chemie – Eugen Werle zum 70. Geburtstag am 10.10.1972. Z Klin Chem Klin Biochem 1972;10:443–4.
15. Hillmann G, Breuer H. Klinische Chemie in der Bundesrepublik Deutschland. Dtsch Ges Klin Chem Mitt 1970;4:3–9.
16. Appel W. Zur gegenwärtigen Situation der Klinischen Chemie und Klinischen Biochemie aus der Sicht eines Industriebiochemikers. Dtsch Ges Klin Chem Mitt 1970;6:7–10.
17. The International Union of Biochemistry and Molecular Biology (IUBMB). Available from: http://www.iubmb.org. Accessed June 2012.
18. About IUPAC. Available from: http://www.iupac.org. Accessed June 2012.
19. History of the IFCC. Available from: http://www.ifcc.org. Accessed June 2012.
20. Schütte E. Joachim Brugsch 65 Jahre. Z Klin Chem Klin Biochem 1974;12:53.
21. Schütte E. Joachim Brugsch zum Gedenken. J Clin Chem Clin Biochem 1981;19:177.
22. Plebani M. Editorial. Preface: Happy 50th anniversary. Clin Chem Lab Med 2013;51:1–2.
23. Stamm D. Johannes Büttner on the occasion of his 60th birthday. Eur J Clin Chem Clin Biochem 1991;29:161–3.
24. Hillmann G, Büttner H. Gründung der Deutschen Gesellschaft für Klinische Chemie. Z Klin Chem 1964;2:128.
25. Körber F, Guder W, Noyer-Weidner M. Johannes Büttner on the occasion of his 65th birthday. Eur J Clin Chem Clin Biochem 1996;34:167–70.
26. Scott T, Brewer M. Concise encyclopedia of biochemistry. Translated into English, revised and enlarged from Brockhaus ABC Biochemie. (Jakubke HD, Jeschkeit H, editors). ©1976, 1981, VEB F. A. Brockhaus Verlag Leipzig; Berlin, New York: Walter de Gruyter, 1983.
27. Publishers' note. Clin Chem Lab Med 2004;42:575.
28. Publisher's note. Clin Chem Lab Med 2011;49:1.
29. Plebani M. Editorial: Thank you, indeed. Clin Chem Lab Med 2011;49:1759–60.
30. Büttner J. Johann Joseph von Scherer (1814–1869). Ein Beitrag zur frühen Geschichte der Klinischen Chemie. J Clin Chem Clin Biochem 1978;16:478–83.

31. Noyer-Weidner M, Büttner J. Friedrich Körber on the occasion of his 60th birthday. Eur J Clin Chem Clin Biochem 1994;32:327.
32. Büttner J. Friedrich Körber 25 years as Managing Editor. Eur J Clin Chem Clin Biochem 1993;31:3.
33. Kornberg A. Understanding life as chemistry. Clin Chem 1991;37:1895–9.
34. Keller H. 50 Jahre Klinische Chemie miterlebt. Ther Umsch 1995;52:298–305.
35. Staudinger Hj. Rückblick und Ausblick. In: Kattermann R, editor. Naturwissenschaft und Medizin: 75 Jahre Klinische Chemie, Pathobiochemie und Endokrinologie in Mannheim 1910–1985. Private Print 1985:195–201.
36. Bergmeyer HU, editor. Methods of enzymatic analysis. Weinheim: Verlag Chemie, vol I–XII, 1983–6.
37. Guder WG. Trends und Zukunftsaspekte der Klinischen Chemie. Mitt Dtsch Ges Klin Chem 1986;17:285–91.
38. Whitehead EC. History of Technicon Corporation. Frankfurt: Technicon Symposium, 1978.
39. Skeggs LT. An automatic method for colorimetric analysis. Am J Clin Pathol 1957;28:311–22.
40. Netheler H. Eppendorf Gerätebau 1945–1970. Firmendruckschrift Netheler & Hinz GmbH, Hamburg, 1971.
41. Sanz MC. Ultramicromethods and standardization of equipment. Clin Chem 1957;31:406–19.
42. Mattenheimer H. Mikromethoden für das Klinisch-Chemische und Biochemische Laboratorium. Berlin: De Gruyter, 1966.
43. Anderson NG. Comments on automation in the clinical laboratory. Z Klin Chem Klin Biochem 1972;10:489–90.
44. Anonymous. Preis Biochemische Analytik 1972. Z Klin Chem Klin Biochem 1972;10:292.
45. Richterich R, Greiner R. Analysatoren der Klinischen Chemie. I. Maschinen, Automaten, Analysatoren, Z Klin Chem Klin Biochem 1970;8:588–94.
46. Richterich R, Greiner R. Analysatoren der Klinischen Chemie. II. Terminologie und Klassifikation. Z Klin Chem Klin Biochem 1971;9:187–93.
47. Richterich R, Greiner R. Küffer H. Analysatoren der Klinischen Chemie. III. Beurteilungskriterien und Fehlerquellen. Z Klin Chem Klin Biochem 1973;11:65–75.
48. Greiner R. Der Greiner Electronic Selective Analyzer (GSA) II. I. Beschreibung aus technischer Sicht. Z Klin Chem Klin Biochem 1973;11:76–86.
49. Richterich R, Küffer H, Lorenz E, Colombo JP. Die Bestimmung der Glucose in Plasma und Serum (Hexokinase/Glucose-6-Phosphat-Dehydrogenase-Methode) mit dem Greiner Electronic Selective Analyzer GSA II. Z Klin Chem Klin Biochem 1974;12:5–13.
50. Küffer H, Richterich R, Peheim E, Colombo JP. Die Bestimmung des Bilirubins in Plasma und Serum als Azobilirubin mit dem Greiner Electronic Selective Analyzer GSA II. Z Klin Chem Klin Biochem 1974;12:294–302.
51. Küffer H, Richterich R, Kraft R, Peheim E, Colombo JP. Die Bestimmung des Chlorids in Plasma und Serum (Quecksilber [II]-Thiocyanat-Methode) mit dem Greiner Electronic Selective Analyzer GSA II. Z Klin Chem Klin Biochem 1975;13:203–11.
52. Miayi K. Advances in non-isotopic immunoassay. Clin Chem 1985;24:61–110.
53. Wisser H, Knoll E, Radke D. Klinisch-chemische Routineanalytik mit vorgefertigten Reagenzienträgern. J Clin Chem Clin Biochem 1986;24:147–54.
54. Dandliker WB, Kelly RJ, Dandliker J, Farquahar J, Levin J. Fluorescence polarization immunoassay. Theory and experimental method. Immunochemistry 1973;10:219–27.
55. Köhler G, Milstein C. Continuous cultures for fused cells secreting antibody of predefined specificity. Nature 1975;256:495–7.
56. Anonymous. Preis Biochemische Analytik 1982. J Clin Chem Clin Biochem 1982;20:531.
57. Mullis KB. AACC Award 1993. Clin Chem 1993;39:1562–3.
58. Anonymous. Prize Biochemical Analysis 1990. J Clin Chem Clin Biochem 1990;28:549.
59. Kattermann R. Kapitel VIII. 1974–1985: Das Klinisch-Chemische Institut in Krankenversorgung, Lehre und Forschung. In: Kattermann R, editor. Naturwissenschaft und Medizin: 75 Jahre Klinische Chemie, Pathobiochemie und Endokrinologie in Mannheim 1910–1985. Private Print 1985:168.
60. Publisher's note. To our readers, authors and subscribers. Eur J Clin Chem Biochem 1997;35:891.
61. Plebani M. The changing face of clinical laboratories. Clin Chem Lab Med 1999;37:711–7.
62. Siest G, Plebani M. CCLM: evolving to meet the needs of today's laboratory professionals and scientists. Clin Chem Lab Med 2008;46:883–4.
63. Plebani M, Marincola FM. Research translation: a new frontier for clinical laboratories. Clin Chem Lab Med 2006;44:1303–12.

Prof. Dr. med. Joachim Brugsch (1909–1980) (see p. 11).

Prof. Dr. med., Dr. rer. nat. Ernst Schütte (1908–1985) (see p. 12).



Prof. Dr. med., Dr. rer. nat. Johannes Büttner (born 1931) (see p. 17).

Prof. Dr. med. Walter G. Guder (born 1938) (see p. 28 and Table 2).

Prof. Gérard Siest received his pharmacy diploma, his specialization in laboratory medicine and his PhD from the Universities of Strasbourg and Nancy. He was Professor of Biochemistry, Molecular Biology and Molecular Pharmacology and in charge of the direction of the Center for Preventive Medicine laboratory, and some years later, for all of the research of this health screening organization. He developed a research team linked to CNRS and INSERM dealing with drug metabolism, more particularly, the UDPGTs and on the genetic influence on laboratory tests and on reference values. Two proteins were studied more deeply: apolipoprotein E and gamma-glutamylstransferase. He created and was in charge of the regional post-graduate course on drug metabolism and biochemical pharmacology. He was President of the European Society of Biochemical Pharmacology and of the International Federation of Clinical Chemistry (IFCC) for 6 years. Gérard Siest was Editor-in-Chief of *CCLM* from 1998 until 2008. In 2010, he founded a new European Society of Pharmacogenetics and Theranostics (ESPT) for which he is now President and Editor-in-Chief of the journal Drug Metabolism and Drug Interactions (DMDI) that is also the official journal of ESPT. In addition, he is involved in many boards of pharmacogenomics and laboratory medicine journals. He has published over 600 peer review publications. The scientific conferences organized every two years, in Santorini (Greece) under his responsibility are very successful.

Prof. Mario Plebani obtained his medical degree summa cum laude from the Medical School of the University of Padua in 1975. He completed residency training and specialization in Laboratory Medicine (1978), and subsequently in Gastroenterology (1983) at the same University. He is full Professor of Clinical Biochemistry and Clinical Molecular Biology at the University of Padua, School of Medicine, Chief of the Department of Laboratory Medicine at the University-Hospital of Padua, and Chief of the Center of Biomedical Research (a specialized Center for quality in laboratory medicine for the Veneto Region). Currently, he is also Director of the Post-graduate School in Clinical Biochemistry at the Medical School of the Padua University and President of the Course for Medical Technologists at the same Medical School. He served as President of the International Society of Enzymology (ISE) for 4 years (2004–2008) and as President of the Italian Society of Clinical Biochemistry and Molecular Clinical Biology for 5 years (in 2003 and from 2007 to 2009). He is the Chairman of the IFCC Working group on 'Laboratory errors and patient safety' (WG LEPS) and in 2008 received the AACC Award for Outstanding *Clinical Laboratory Contributions to Improving Patient Safety*. Dr. Plebani is Editor-in-Chief of *CCLM,* and Associate Editor of CRC Clinical Laboratory Sciences, and International Journal of Biological Markers. His main areas of research are quality in laboratory medicine, biomarkers in cancer and cardiovascular diseases, and in vitro allergy diagnostics.

Prof. Friedrich Körber, born May 2, 1934 in Petlau/Zittau, Upper Lusatia, attended primary school in Waltersdorf, Upper Lusatia (1940–1944), and academic high school (Gymnasium) in Zittau, Saxony (1944–1949). In 1949, his parents started a new life phase in the rural area near Halle/Saale, and Friedrich became a student of the Francke Foundation in Halle/Saale. After the matura in 1952, he did not obtain the concession to go to university (medical faculty). First, he was urged to prove to be a loyal citizen of the communist social system by working in the industry. He worked as a laboratory assistant in the school for chemical professions at the Agfa Wolfen Film Factory (1952–1953) and at the Zörbig Hospital Clinical Laboratory and Radiation Division (1953–1954). The final rejection of admission to university gave rise to his change to Berlin (West), where, after a further year at school, he was admitted to the Free University of Berlin. He studied medicine (1955–1961), graduated in medicine (Dr. med., 1964) with a thesis on carbonic anhydrase. Thereafter, he studied a Postdoctorate at the Institute for Molecular Biology and Biochemistry (1964–1979), received habilitation in Physiological Chemistry and Clinical Chemistry (1970), and became Professor in 1970. He had the leading position at the Central Institute for Biochemistry and Biophysics at the Free University of Berlin, and developed curricula for the Diploma in Biochemistry and Medical Physics, 1970–1976. He was Dean of the Faculty for Basic Medicine (1977–1995), and Professor emeritus in 1999. After the fall of the Berlin Wall in 1989, he undertook various activities under the roof of the German heritage protection foundation in Upper Lusatia/Lower Silesia: Waltersdorf, Herrnhut/Berthelsdorf, Goerlitz, and Reichenbach. He has been an examiner in Biochemistry since 1970 until today and was the Managing Editor of this *Journal* from 1967 to 1997.