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Eponyms in clinical chemistry

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ABSTRACT

Background: Eponyms are commonly used in medicine, but there are no specific studies of the use of eponyms in clinical chemistry.
Methods: Clinical chemistry eponyms were manually collected from books, review articles and journal articles from 1847 through 2020. Eponym usage was examined by searching titles and abstracts in PubMed. Custom Python scripts were used to first permute eponyms into multiple forms, and then to search PubMed using Biopython. The eponyms identified in PubMed were further focused on 2 clinical chemistry journals *Clinica Chimica Acta* [CCA] and *Clinical Chemistry* [CCJ].
Results: The manual collection identified >300 eponyms in clinical chemistry. The Biopython search of PubMed identified a subset of 97 unique eponyms in 33,232 articles. PubMed identified 26 eponyms used in 130 CCA articles; whereas a full-text search identified 1187 articles. In comparison, PubMed identified 36 eponyms used in 158 CCJ articles; whereas a full-text CCJ search identified 708 articles. PubMed shows that the journals CCA and CCJ had a peak number of eponym citations in 1977 followed by a steady decline.
Conclusions: Eponyms have been frequently used in clinical chemistry with 97 eponyms in common use in PubMed. Overall, the use of clinical chemistry eponyms appears to be declining.

1. Introduction

Naming chemical reactions, chemical reagents, mathematical equations, units, coefficients, constants, laws, diseases, and clinical signs and symptoms, after people (eponyms), places (toponyms) or mythical beings (mythonyms) is not uncommon, and there are a number of compendia of medical eponyms [1–3]. Likewise, in the field of clinical pathology there are compendia of eponyms used in hematology [4], and microbiology [5], but we are not aware of a compendium of eponyms relating specifically to clinical chemistry. There are some general works published at the end of the 19th century and the beginning of the 20th century that list named "tests (reagents)" [6], reagents and reactions relevant to physiological-pathological chemistry [7], pharmacology/toxicology [8], "tests and reagents known by their author's names" of practical utility for "the busy chemist, microscopist, and pharmacist" [9], and reactions and reagents for the doctor, analyst, pharmacist, and chemist [10]. Although these lists contain some clinical chemistry eponyms, by and large, they are general lists with an emphasis on chemistry tests and reagents.

Eponyms abound in clinical chemistry, including some derived from general laboratory sciences (e.g., Erlenmeyer flask), or from the intersection of clinical chemistry with physics (e.g., Rayleigh scattering), biochemistry (e.g., Michaelis-Menten kinetics), and statistics (e.g., Kruskall-Wallis test). Recently, we examined the natural history of the Malloy-Evelyn Reaction, and traced the coinage and chronology of the adoption of this eponym [11]. We have now extended our study of eponyms and have compiled a list of eponyms relating specifically to clinical chemistry methods, tests, reagents, apparatus, tables, formulae, and coefficients, and examined their usage in clinical chemistry over time.

2. Materials and methods

2.1. Collection of an index of clinical chemistry eponyms

An index of clinical chemistry eponyms was created from a search of

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83 textbooks, handbooks, manuals, and reviews (published between 1847 and 2018) (Supplemental Table 1). We manually searched these publications, with an emphasis on the tables of contents and indexes. We also searched various books that comprise alphabetical lists of named reagents, reactions and tests dating to the period 1885–1909 [6–10]. From this earlier period, many lists include named reactions or reagents used for testing clinical specimens (e.g., urine), but these did not appear in any of the clinical chemistry textbooks that we searched. This earlier period had eponyms that, by the admission of one author, were only "occasionally quoted by the author's name" [8]; accordingly, we have not included these more obscure eponyms from 1885 to 1909 in our analysis. In addition to the eponyms in published texts, eponyms from article titles in the journal *Clinical Chemistry* (CCJ) were included (February 1955 to July 2020).

2.2. PubMed search

The index of clinical chemistry eponyms was then used to search PubMed. Custom python scripts were developed using Biopython's Entrez module [12]. The overall data flow is illustrated in Supplemental Fig. 1, and the scripts and data are publicly available on github (https://github.com/cornish/pubmed-eponyms). Briefly, the original list of clinical chemistry eponyms was edited to split surname and test/reagent type into separate columns in a comma-separated values (CSV) file. Terms in which multiple surnames were separated by spaces were converted to separation by hyphens to disambiguate them from surnames having multiple parts (e.g. "Van Slyke"). Two terms (Friedewald, Kjeldahl) had duplicates (possessive v. non-possessive) removed. A script then standardized the eponyms by removing all possessives and separating multiple surnames using hyphens. A second script permuted the standardized terms to create an exhaustive list of possible variations that might appear in the literature (see Supplemental Fig. S2). As an example, the term "Adler Test" generated the variants "Adler's Test," and "Test of Adler" in addition to the original term. The Biopython library was then used to search PubMed (search performed on August 12, 2020) for exact phrase matches of the permuted terms in titles or abstracts, replicating a standard PubMed search. Duplicate citations appearing for each original term were removed. The eponyms were examined for trends across journals over time.

2.3. Full text search

From the PubMed based search, a focused examination was performed on 2 of the oldest clinical chemistry publications: *Clinica Chimica Acta* (CCA) and *Clinical Chemistry* (CCJ). The use of the eponyms was quantified for each journal, and then an additional search was performed within the full-text search engines on the journal websites (full-text searches on September 7, 2020) [13,14].

3. Results

3.1. Index of eponyms.

A total of 323 clinical chemistry eponyms were collected (Supplemental Table 2). For each eponym, we include the date of the original work, as the earliest possible date for the eponym, and reference(s) to the original work. The chronological distribution of the eponyms is as follows: 1800–1849 (n = 8); 1850–1899 (n = 110); 1900–1949 (n = 150); 1950–2000 (n = 55) and reveals a peak coinage in the first half of the 20th century. The oldest eponym in this collection is the Gmelin's Test for bile pigments which is based on work from 1826 [15]. The most recent is the Matuszewski Method for assessing matrix effects in LC/MS/MS method based on work from 1998 [16]. The largest number of eponyms were for glucose or sugar tests (~15% of total number of eponyms).

3.2. PubMed search

Automated searching of the PubMed database using Biopython expanded the 323 eponyms into 1499 permutations (e.g., "Adler Test", "Adler's Test", "Test of Adler") (Fig. 1). This query of PubMed identified a total of 34,271 citations which were reduced to 33,232 when duplicate citations were excluded. Only 97 of the 323 eponyms in our index were identified in PubMed by the various permutations. The most commonly occurring eponyms in PubMed were "Southern Blot" (n = 17,667), "Sanger Sequencing"/"Sanger's Sequencing" (n = 10,231), and "Friedman Test"/"Friedman's Test" (1907). These top three eponyms accounted for 89.7% (29,805 of 33,232) of PubMed results.

Within the PubMed search results, several problems in the eponym search strategy were identified. Notably, the "Friedman Test" is a pregnancy test from the early 20th century; however, the majority of citations in PubMed for "Friedman Test" are for a non-parametric statistical test of the same name [17]. Several other eponyms such as "Weber Test" and "Robin Test" were also found to have mistaken identity in eponymous usages outside of the clinical laboratory. Other terms such as "Legal Test" are general non-eponymous terms used without reference to an individual. In addition, spelling errors were identified such as the frequent incorrect spelling of the "Friedewald Formula" as "Friedwald Formula", or even "Fried Wald Formula". Another misspelled eponym was the "Kjeldahl Method" often misspelled as the "Kjedahl Method". Excluding "Sanger Sequencing", "Southern Blot", and eponyms with mistaken identity, the top eponyms in the PubMed search were "Folin-Ciocalteu Method" (n = 438), "Cockcroft-Gault Equation" (n = 369), "Lowry Method" (n = 322), "Friedewald Formula" (n = 295), "Kjeldahl Method" (n = 216), "Jaffe Reaction" (n = 193), "Guthrie Test" (n = 135), "Berthelot Reaction" (n = 65), "Van Slyke Method" (n = 48), and "Rumack-Matthew Nomogram" (n = 44).

The journals which use clinical chemistry eponyms were also investigated within the PubMed search. Including all eponyms, the top ten journals with citations were: *PLoS One* (n = 584), *Proceedings of the*

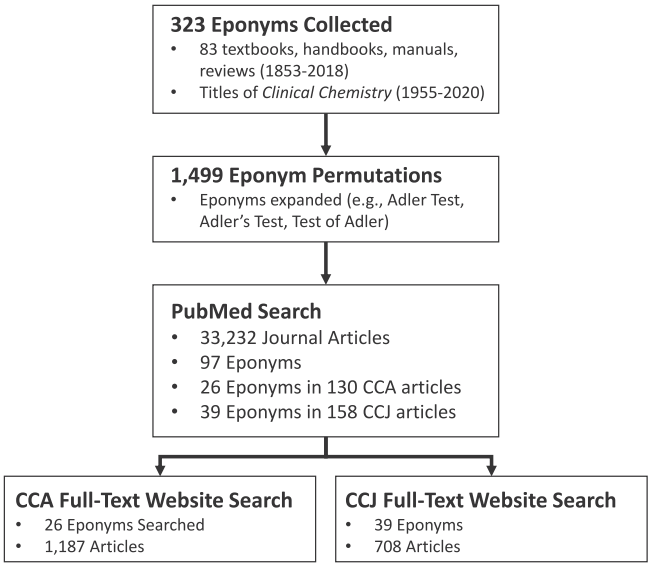

Fig. 1. Eponyms in the Study. An initial set of 323 eponyms were identified. Variations on these eponyms were generated, resulting in 1499 terms which were then searched in PubMed using Biopython. The 1499 terms identified 33,232 journal articles. Of the original 323 eponyms, only 97 were identified in PubMed. In the journals *Clinical Chemistry* (CCJ) and *Clinica Chimica Acta* (CCA) 39 and 26 eponyms were seen in PubMed, respectively. These subsets of eponyms were then searched in each journal's full-text search engines. The CCA PubMed search identified 130 articles where as full-text search identified 1187 articles. Similarly, the CCJ PubMed search identified 158 articles containing eponyms whereas full-text search identified 708 articles.

National Academy of Science USA (n = 440), *Gene* (n = 417), *Journal of Biological Chemistry* (n = 379), *Chinese Journal of Medical Genetics* (n = 348), *Blood* (n = 310), *Plant Molecular Biology* (n = 275), *Genomics* (n = 272), *Plant Cell Reports* (n = 272), *Journal of Bacteriology* (n = 240), and *Cancer Research* (n = 235). Excluding Sanger Sequencing, Southern Blot and Friedman Test showed the top ten journals as: *Clinical Chemistry* (n = 126), *Journal of Agricultural and Food Chemistry* (n = 68), *Analytical Biochemistry* (n = 66), *Clinica Chimica Acta* (n = 57), *Talanta* (n = 42), *The Biochemical Journal* (n = 38), *Molecules* (n = 30), *Clinical Biochemistry* (n = 29), *Annales de Biologie Clinique (Paris)* (n = 26), and *Food Chemistry* (n = 25).

3.3. PubMed searches of CCA and CCJ.

The eponym search was then focused on the 2 oldest journals in clinical chemistry: CCA and CCJ. In PubMed there were 130 articles representing 26 eponyms in CCA, and 158 articles representing 39 eponyms in CCJ. The combined list of frequently used eponyms in these 2 journals is similar to that seen in the search of PubMed across all journals (Table 1). In most years, there were less than 10 PubMed eponym-containing citations for CCA and CCJ combined. When Southern Blot and Sanger Sequencing are excluded, there have been less than 5 PubMed citations per year for CCA and CCJ combined since 1991.

3.4. Full-text search of CCA and CCJ

Although the usage of clinical chemistry eponyms in PubMed appears to be limited, the PubMed queries are limited to the title and abstract of articles. To examine the prevalence of eponym usage throughout an article, the full-text article web-based search engines for each journal were used. Interestingly, both CCA (ScienceDirect/Elsevier) and CCJ (Oxford University Press) have web-based search engines that automatically include terms with and without the possessive apostrophe "s". For example, CCJ has 100 results for Friedewald Formula and the identical 100 results for Friedewald's Formula. Full-text search of the CCA for the 26 eponyms from PubMed identified 1187 articles; 9.3-fold (1187/130) more articles than PubMed. Similarly, for CCJ, the 39 eponyms identified in PubMed were searched across the full-text of the journal and identified 708 articles; 4.5-fold (708/158) more articles than PubMed. These finding are to be expected in view of the more complete nature of full-text searching rather than a query limited to the title and abstract (PubMed).

Table 1
Combined and ranked, eponyms from a PubMed search of *Clinical Chemistry* and *Clinica Chimica Acta*.

Rank	Eponym (year of publication of original work)	Citations*
1	Sanger Sequencing (1977)	75
2	Jaffe Reaction (1886)	33
3	Friedewald Formula (1972)	32
4	Southern Blot (1975)	28
5	Jendrassik-Grof Method (1938)	13
6	Kober Reaction (1931)	9
7	Berthelot Reaction (1859)	8
8	Liebermann Burchard Reaction (1889)	8
9	Zimmerman Reaction (1935)	8
10	Trinder Method (1969)	7
11	Abell-Kendall Method (1952)	6
12	Lowry Method (1951)	6
13	Kjeldahl Method (1883)	5
14	Pisano Method (1960)	5
15	Allen Correction (1950)	4
16	Natelson Microgasometer (1951)	3

*Only eponyms with more than 2 usages in PubMed from the 2 journals combined are listed.

3.5. Chronology

In relation to time, the earliest article identified in the PubMed search was for the term "Legal Test" in 1867; unfortunately, this usage was not for a clinical laboratory test, that dates back to 1882 (Supplemental Table 2), but rather for a legal test of a law. From 1867 to 2019 the growth in eponym citations in PubMed has 2 peaks, an initial peak of 1023 articles was identified in the year 1994 which then dropped to a low of 433 in 2008 (Fig. 2). Subsequently, eponym usage increased to 2142 in 2019, the most recent complete year studied. The 2 highest cited eponyms were "Southern Blot" (17,667) and "Sanger Sequencing" (10,231). Beginning in 1978, "Southern Blot" grew to a peak annual citation of 966 in 1994 (Fig. 3). Thus, the 1994 peak of overall PubMed citations was 1023 of which 966 were for the term "Southern Blot". Usage of the Southern Blot eponym declined after 1994 to only 100 citations in 2019. In comparison, Sanger Sequencing appeared in PubMed in 1985 and has continuously grown in usage to the present time with 1747 citations in 2019.

When the use of the eponyms (excluding Southern Blot and Sanger Sequencing) is examined for the journals CCA and CCJ the usage in PubMed shows that the peak number of eponym citations was in 1977 with 14 citations, with steady decline since that year. In 2019, there was only one eponym used in titles or abstracts in these 2 journals. Full-text searching of CCA and CCJ over time was not examined.

4. Discussion

Clinical chemistry research work originating in the last half of the 19th century and the first half of the 20th century produced the largest number of eponyms. The latter half of the 20th century has seen a significant decline in the coinage of eponyms. The generation of our list of eponyms (Supplemental Table 2) involved various forms of searching, beginning with manual searches of hardcopy or electronic resources (e.g., e-books) and transitioning to electronic searches of online full-text journals. The eventual scale of our PubMed searches for our entire collection of 323 eponyms was facilitated by automated scripting in Python. Biopython's Entrez module was used because it simplifies many aspects of accessing the NCBI's E-utilities application programming interface (API) for searching Entrez databases (including PubMed). [18]. Other studies of medical eponym usage have included semi-automatic text mining to extract eponyms from a full-text publication [19], and "webscraping" to search PubMed (1900–2014) [20]. Interestingly, the latter study showed a steady increase in the number of uses, a decline in the prevalence of usage, and a loss in medical eponym diversity (i.e. fewer eponyms in active use over time). Notably, one must be very careful when using PubMed to identify citations for laboratory eponyms due to the default behavior of PubMed when no matches are found for a quoted phrase. In these instances, PubMed will still try to return results by breaking up the quoted phrase. In an extreme example, searching for the quoted phrase "Almen-Bottger Test" returns no exact matches. PubMed then translates the search string to "Almen-Bottger AND Test" which also returns no matches. PubMed then drops "Almen-Bottger" (because it doesn't appear in the PubMed database) and simply searches "Test", which returns 1,489,563 results. For this reason, we elected to reject all results in which the exact quoted phrase was not matched.

An interesting finding from our analysis of the use of eponyms, as evidenced by citations in PubMed, has been the prominence of the Southern Blot and Sanger Sequencing. These 2 eponyms are the major contributors to increasing eponym usage. An argument could be made that these eponyms belong to the laboratory medicine sub-specialty of Molecular Diagnostics. However, our analysis shows that these eponyms are widely used in the clinical chemistry literature, and this perhaps speaks to the blurring of the borders between the sub-specialties in laboratory medicine. Their removal from our search reveals that overall use of eponyms in clinical chemistry is infrequent and may be in decline.

The eponymous fame, conferred on the scientists listed in Table 1,

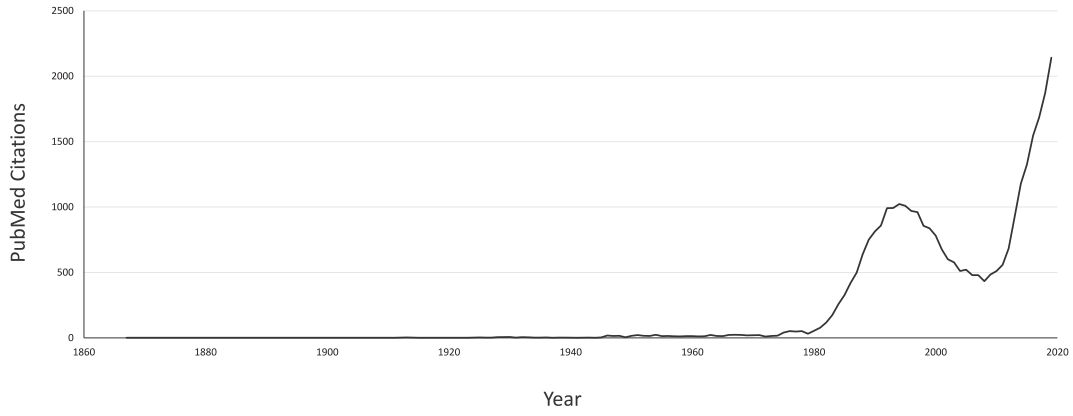

Fig. 2. PubMed citations containing clinical chemistry eponyms. The frequency of clinical chemistry eponym citations in PubMed is shown from 1867 to 2019. There is an initial peak of 1023 citations in 1994, and a subsequent decline to a low of 433 in 2008. Subsequently, there has been annual growth to 2142 in the latest full year examined (2019).

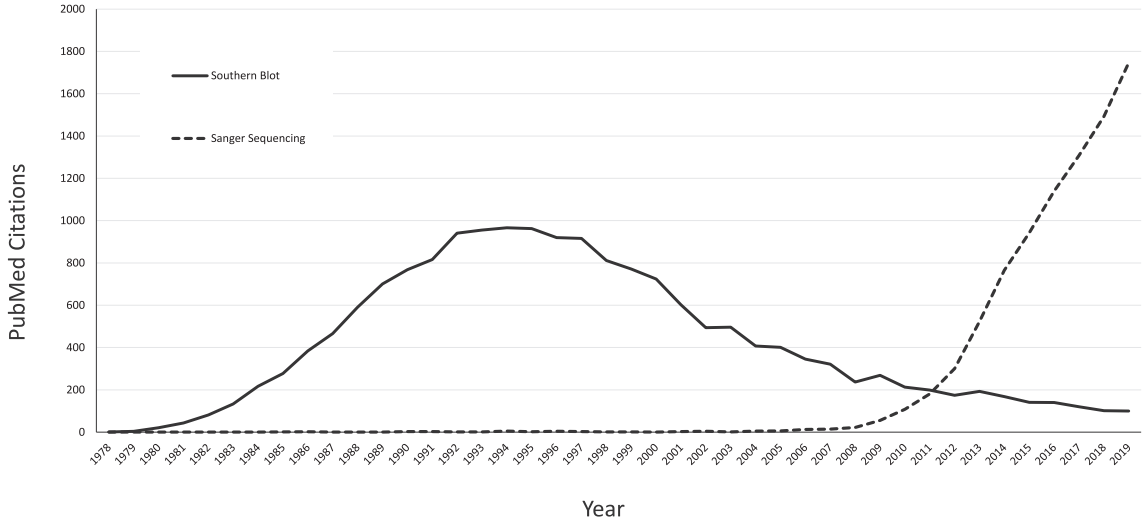

Fig. 3. Southern Blot and Sanger Sequencing Eponyms: Usage in PubMed. The number of PubMed indexed journal articles with the eponyms present in their title or abstract were enumerated. Southern Blot first appeared in PubMed in 1978, reached a peak of 966 occurrences in 1994, and declined to 100 occurrences in 2019. Sanger Sequencing first appeared in PubMed in 1985 and has increased to 1,747 occurrences in 2019.

has in some cases been accompanied by success marked with prizes (e.g., Nobel Prizes to Sanger; Lasker Award to Southern), and "royal honours" (see Supplemental Table 4). However, whilst there are extensive biographies of many of these researchers, for some there is scarcely any biographical information available, beyond what can be inferred from their affiliation listed in their published work.

In recent years there have been arguments for [21] and against the use of eponyms [22]. Arguments against include ethical arguments based on the actions or political affiliations of the scientist [23]. Less serious concerns have related to stylistic issues centering on the possessive and non-possessive forms of eponyms (i.e., to use of not to use an apostrophe "s") [24,25]. Nevertheless, despite these contrary opinions and concerns, eponyms continue to remain an established part of science and medicine, generally, and in clinical chemistry in particular.

Credit authorship contribution statement

Larry J. Kricka: Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing - original draft, Writing - review & editing. **Toby C. Cornish:** Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing - review & editing. **Jason Y. Park:** Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing - original draft, Writing - review & editing.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cca.2020.11.014.

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