Is Crohn's disease a rightly used eponym?

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Abstract

In 1932 Burrill B. Crohn, a gastroenterologist at Mount Sinai Hospital in New York City described, together with two surgical colleagues, a series of 14 patients with an inflammatory condition of the terminal ileum. All patients were operated on by Dr Albert Berg, the Chief Surgeon of the hospital, whose name did not appear on the initial publication. The "new" disease was called "regional ileitis", but was rapidly referred to as "Crohn's disease". From earlier accounts and publications it has become clear that the condition had already existed for many centuries and was "discovered" several times before 1932, most notably (amongst others) by Giovanni Morgagni in 1769, Antoni Lesniowski in 1903 and Thomas K. Dalziel in 1913. 'Crohn's disease' might reasonably be known by another eponym. Nevertheless, the 1932 publication of Crohn was pivotal, as were his later contributions to the knowledge of "his" disease. Therefore the worldwide use of the eponym is rightly to be continued. Present researchers and clinicians with an interest in IBD might learn from the complicated story recounted in this contribution. Apart from an interesting historical overview, there are some lessons for today: the importance of thorough clinical observation and pattern recognition, the need for communication between colleagues and of multidisciplinary approaches, the need for broad access to valuable data, past or present, regardless of the journal or language of publication. It should ultimately bring us some humility despite great achievements in treating this chronic disease, which defies all our efforts yet to find a cure.

Keywords

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An eponym is the name of an object named after a person, usually to honour the person for his or her contribution to the discovery or development of the object. With "real" eponyms, which are no longer written with a capital letter, such as zeppelin, diesel or pasteurization, virtually no one thinks of the original person (respectively Ferdinand Graf Zeppelin, Rudolf Diesel and Louis Pasteur). Medical jargon is littered with eponyms and their use is controversial (**1**). Eponyms often provide a less than truthful account of how diseases were discovered. On the other hand, they might increase interest in medical history and their analysis may lead to a more accurate understanding of scientific discoveries, let alone individual contributions.

In gastroenterology, Crohn's disease is one of the most famous eponyms. The history of inflammatory bowel disease has been told and re-told comprehensively (**2,3,4**), but this article will focus on Dr Crohn and the question of whether his name is most appropriately associated with the illness after whom it has become named.

The 1932 publication

Burrill Bernard Crohn **(fig.1**) was born in New York on 13 June 1884, one of 12 children in a Jewish emigration family of German descent. After studying medicine at the renowned Columbia University where he received his MD degree in 1907, he specialized in internal medicine at Mount Sinai Hospital and spent the rest of his career as a gastroenterologist in this hospital, in his hometown. He died at almost 100 years of age in 1983 (**5**).

Crohn was interested in, among other things, inflammatory diseases of the gut. In 1925 he was the first to describe a case of a tumour in a patient with ulcerative colitis (**6**). On 2 May 1932, Crohn gave a presentation on 14 patients with "terminal ileitis" to the annual meeting of the American Gastroenterological Association (AGA). All patients had nonspecific inflammation (i.e. not caused by known bacteria, such as tuberculosis) of the last segment of the small intestine, the terminal ileum. At the suggestion of one of the attendees, the name “terminal” ileitis was replaced by regional ileitis, to avoid the impression that the disease was always lethal. Indeed, it was observed that the condition could sometimes be successfully treated by surgery.

Following this presentation, Crohn published an article in the *Journal of the American Medical Association* (JAMA) together with Leon Ginzburg and Gordon Oppenheimer, presenting regional ileitis as a “new” disease (**7**). The article included a precise clinical description of the condition, with details of complications, such as stenosis, fistulae and perforation. It was also illustrated with radiological images. All patients were treated in a surgical manner and medical treatment was dismissed in a single sentence as "purely supportive and palliative".

All 14 described patients, aged between 17 and 52, had been operated on by Dr. Albert A. Berg (1872-1950) (**fig.2**), Senior Consulting Surgeon at Mount Sinai Hospital **(8).** 'AA' (Albert Ashton) was of Hungarian stock and his name is sometimes wrongly cited as Alexander; his elder brother Henry was another doctor and together they established a spectacular collection of books in New York's Public Library [ref]. Ginzburg and Oppenheimer, both of whom were working respectively as an adjunct surgeon and as a pathologist with Berg, had collected data from 12 patients who had been operated on by Berg from 1920 onwards for inflammation and consequent obstruction of the terminal ileum, in which infectious causes had been ruled out as far as possible. The interest of Crohn had been aroused by certain clinical observations upon 2 patients of his own with a similar condition, also operated on by Berg. Crohn was Berg's Medical Consultant. The hospital's Chief Pathologist, Paul Klemperer, who had supervised the pathological studies on all the resected bowel segments, encouraged everyone to bring their data together in one publication. It is unclear if Crohn submitted the manuscript with his name first, but at the time it was *JAMA's* policy to order authors alphabetically.

The man who had actually treated all the patients (Berg), did not wish to be mentioned, because he had not previously been involved in the publication project (**9**). In 1951 Ginzburg recalls in an article in memory of Berg how the latter stimulated him to study and clarify the subject of inflammatory lesions of the bowel and concludes that "*Dr Berg is not usually associated with this condition*. *There is a certain injustice in this"* **(10).** If Berg's name had appeared on the article in alphabetical order, we would be talking about *Berg's disease* today.

This seminal publication in 1932 is widely regarded as the first description of a new clinical entity: Crohn's disease. But such regard is wrong.

"Crohn's disease" before 1932 ?

Crohn, Ginzburg and Oppenheimer were by no means the first to describe this syndrome. There are a surprising number of clinical cases and autopsy reports from the 17th Century and perhaps even earlier, describing symptoms and pathological findings compatible with 'Crohn's disease'. The great anatomist *Giovanni Battista Morgagni* (1682-1772) mentioned in 1769 a possible case in his collection in 5 volumes of all known disorders: *"De sedibus et causis morborum"* ("About the localization and causes of diseases") (**11**). He described a 20-year old male patient who died following a longstanding illness with fever, abdominal pain and bloody diarrhoea. On autopsy, transmural inflammation and perforation were revealed from the terminal ileum to "two hands breadth" along the colon.

Even earlier, it is suspected that the French king Louis XIII, who died in 1643 at the age of 42, might have had Crohn's disease. After many years of remitting and relapsing complaints of abdominal pain, diarrhoea and joint pain, he eventually died after an episode of very severe abdominal pain. Inflammation of the small intestine with perforation and peritonitis was observed at the autopsy. A concomitant pulmonary cavity raises the suspicion of tuberculosis as a differential diagnosis (**12**).

The British physician *Sir Samuel Wilks*, FRS, PRCP published a case report in 1859 about '*The morbid appearance in the intestine of Miss Bankes*', a case which is usually regarded as the first description of ulcerative colitis but which, in retrospect, is difficult to differentiate from colonic Crohn's disease (**13,14,15**). The lesions in the colon are described as: "*these (ulcers in the colon) may be isolated scattered over the membrane, but more usually they are united and form a continuous serpentine ulceration throughout the large bowel.*

Albert von Sachsen-Coburg, Prince-Consort of Queen Victoria, died in 1861, also aged 42, officially of typhoid fever. Thorough examination of diaries and medical reports lead to the conclusion that his condition was more likely that of chronic intestinal disease, such as Crohn's disease, as suggested in a recent book (**16**). Since the Queen refused an autopsy on her husband, a final diagnosis will never be possible.

These and other historical cases not discussed in detail here (**17-20**) of patients with fever, pain in the right lower abdomen, diarrhoea and weight loss, always give rise to a difficult differential diagnosis, including intestinal tuberculosis or malignant tumours and lymphoma in particular. In the absence of modern imaging techniques, the correct nature of these earlier cases can never be confirmed with certainty.

From the very beginning of the 20th Century, further publications pointed to an accelerating pace in the existence of a new entity. The Warsaw-based surgeon *Antoni Lesniowski* (1867-1940) described and illustrated (**fig.3**) in 1903 some patients with inflammatory and stricturing lesions of the small intestine, including one with a fistula to the colon. He is still regarded in Poland as the first author to have described Crohn's disease (**21).** In his country whose Gastroenterology Society (Societas Gastroenterologiae Polonia) was founded in 1909, only 12 years after the American Gastroenterology Association (1897) and predating the British Society of Gastroenterology (1937) by 28 years, the entity was called until recently "Lesniowski-Crohn's disease".

The Scottish surgeon *Thomas Kennedy Dalziel* (1861-1924) **(fig.4**) published findings in 1913 on 9 patients with chronic diarrhoea that he operated on because of inflammation and obstruction of the small intestine (**22**) : "*The affected bowel has the consistence and smoothness of an eel in a state of rigor mortis and the glands, though enlarged, are evidently not caseous"*. Dalziel also noted involvement of the colon, something that Crohn initially did not do. Almost certainly these were patients with Crohn's disease, at least some of them. Because the publication appeared just before the First World War, during which the medical world had other concerns, his findings had little resonance and impact. His conclusion is interesting: *"I can only repeat that the aetiology of the condition remains in obscurity but I trust that ere long further consideration will clear up the difficulty".* Unfortunately this has not proved to be the case, although by a quirk of coincidence, 1913 was also the year that *Mycobacterium paratuberculosis*, today called *Mycobacterium avium* subspecies para-tuberculosis (MAP), was described as the cause of Johne's disease in cattle. MAP has been suspected in the past as a cause of Crohn's disease **(23).**

In the 1920s and 30s, publications presenting cases with so-called 'pseudo-tumoral' lesions in the bowel or "tuberculosis without tuberculous bacilli", or non-specific granulomatous bowel inflammation, proliferated. For example, *Eli Moschowitz* (1879-1964) described in 1923,

working as a pathologist in the Beth Israel Hospital in New York and later at the same Mount Sinai Hospital where Crohn worked, 4 patients with such a condition (**24**). We have to assume that Crohn was not aware of this publication, which may not be such a major oversight, with Index Medicus (established in 1879), in its user-unfriendly paper version and the future possibilities of PubMed undreamed of. It does, however imply lack of collaboration or discussion with colleagues, since Crohn had himself published a report on the sigmoidoscopic appearance of ulcerative colitis (6) in the same journal, only 2 years after Moschowitz's cases.

After 1932 : understanding a new disease and birth of an eponym

It took until 1932 before Crohn, Ginzburg and Oppenheimer submitted Berg's groundbreaking series of cases for publication. The article appeared at the right time and in the widely read *Journal of the American Medical Association*. As so often in major advances in science or medicine, all earlier work had prepared the terrain. Dr. Crohn initially thought of "his" disease as a particularly Jewish disease, reputedly joking to other doctors that the ailment was brought on either by "Jewish genes, Jewish food, or Jewish mothers". It is obvious today that the disease occurs worldwide regardless of race or descent, but with striking differences in incidence, probably linked to local external factors. It is now recognized as a disease of industrialized societies and rapidly becoming more frequent in so-called "emerging" countries.

It is striking that in the publication of 1932, only patients with disease in the terminal ileum are described. It soon became clear that other parts of the gastrointestinal system could also be affected. As early as 1933, colonic damage was described, which Crohn initially did not accept as part of the condition. Although Crohn himself, together with Berg, described colonic lesions together with regional enteritis **(25**), it was not until the 1950s and 60s that the existence of "Crohn's colitis" was generally accepted as an entity distinct from ulcerative colitis **(26).** Involvement of other small bowel segments (1936), stomach (1939), mouth (1972) and duodenum (1980) were described later.

Crohn probably did not expect that the eponym would belong to him. The 1932 article proposed to call the disease "regional enteritis". However the "new" disease entity was already referred to as "Crohn's disease" in Great-Britain in 1936 in an article by Barbour (**27**). The eponym was quickly accepted in Scandinavia, but this happened a bit more slowly in the United States, although in 1933 Harris mentioned it in the title of an American publication (**28**). After all, "A prophet not without honour, save in their own country".

Conclusion

On the question whether Crohn's disease is rightly named after Burrill Crohn, the following can be concluded.

- The disease has existed for centuries albeit in a small number of individuals. Indications in this regard are frequently present, but the diagnosis can never be proved.

- The condition has been "discovered" several times (Morgagni, Wilks, Lesniowski, Dalziel and probably others) before a clear description of a separate clinical entity finally appeared. The publication of Crohn and his two colleagues in 1932 can nevertheless be regarded as a milestone. They brought insights and guidance to define and recognize the clinical picture.
- Crohn remained active afterwards and spent a lot of time traveling to speak about "his" disease. From 1934 onwards until 1967, he continued publishing on “regional enteritis”, never calling it Crohn’s disease himself **(29,30)**. He undoubtedly contributed greatly to increasing the knowledge and worldwide interest in the disorder. Therefore, the fact that his name remains connected to the disease is certainly not wrong, but it could just as well have become Berg's disease, or be known as Dalziel’s disease with pleasing alliteration.
- In December 1982, a few months before his death at almost 100 years of age, Crohn, questioned on this issue, replied by telling his story and concluding : *"... but all this is now ancient history".*

In our opinion, knowledge of this “ancient history” is worthwhile for all physicians involved in the care of patients with IBD. What was achieved by pattern recognition in times with far fewer diagnostic tools, illustrates that thorough clinical observation is a powerful instrument and remains an essential clinical skill. It also shows that scientific progress needs multidisciplinary collaboration and is the result of the work of many.

Although our knowledge of inflammatory bowel diseases has increased greatly since 1932, this past history might reasonably induce some humility. When Dalziel in 1913 wrote that “*the aetiology of the condition remains in obscurity but I trust that ere long further consideration will clear up the difficulty”*, more than 100 years later the aetiology and pathogenesis of Crohn’s disease are still unclear, many unmet needs remain and a definitive cure for the disease remains beyond the horizon.

The translated words of the French philosopher René Descartes (1596-1650), who frequently published his thoughts on medicine and science **(31)** are still valid: *“All at present known in medicine is almost nothing in comparison with what remains to be discovered”*. To our minds that is a challenging and stimulating conclusion from this ancient history.

Conflicts of interest

None

Author contributions

Both authors contributed equally to the content and drafting of this manuscript and have approved the final version.

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