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John Goodsir: discovering *Sarcina ventriculi* and diagnosing Darwin's dyspepsia

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Abstract

In 1842, when John Goodsir was Conservator to the Museum of the RCSEd, he saw a 19-year-old male patient who vomited a large volume of acidic, fermented-smelling, watery fluid every morning. Under his microscope, Goodsir found the vomitus to be populated with a micro-organism he named *Sarcina ventriculi*, which he considered to be causative. In so-doing, Goodsir became one of the first people to link a specific micro-organism with a disease. Goodsir recommended small doses of creosote as an antiseptic and claimed that the boy was eventually cured of the vomiting condition. In August of 1863 Charles Darwin was hugely celebrated by the scientific community and the public, but he had suffered from severe stomach problems all his adult life and at this point, he was vomiting daily. He read Goodsir's paper and contacted him and asked if he could send some vomitus samples to Edinburgh in the hope that Goodsir might find *Sarcina* in it and solve the mystery of his debilitating stomach symptoms and perhaps cure them with creosote. Goodsir examined samples in his microscope, but failed to find *Sarcina*. Sadly, Darwin went on to suffer constantly from severe stomach problems, recently attributed to lactose intolerance, until he died in 1882, some 20 years later.

Keywords

John Goodsir, *Sarcina ventriculi*, water brash, dyspepsia, Charles Darwin

John Goodsir

John Goodsir (1814–1867) was born in Fife into a family of high medical achievers (Figure 1). His father and grandfather were doctors and three of his brothers also practised medicine.[1] One of his brothers was Harry Goodsir, a respected researcher and anatomist who was briefly Conservator of the Museum of the RCSEd. He perished in the artic, along with the rest of the crews of HMS Erebus and HMS Terror, on the ill-fated Franklin expedition. John Goodsir first attended St Andrews University in 1827 at the remarkably young age of 13 and was then apprenticed to the surgeon Robert Nasmyth in Edinburgh in 1830.[1,2] At the same time, he enrolled in Edinburgh University Medical School and attended lessons at the Royal College of Surgeons of Edinburgh (RCSEd). He also joined the extramural anatomy classes of Robert Knox, then the greatest of the Edinburgh anatomists, who became his patron and supporter. He became a Licentiate of the RCSEd in 1835, at the age of 21 and as his reputation as an anatomist grew, he became Conservator to the Museum of the RCSEd in 1841. In 1843, he was appointed Curator of the University of Edinburgh anatomy collection, while Harry Goodsir took over Conservatorship of the anatomy museum of the RCSEd. In 1846, John Goodsir was appointed Professor of Anatomy in Edinburgh University in succession to Alexander Monro *tertius* (1773–1859).[1,2] Throughout this time, Goodsir had published on a wide variety of biological and anatomical topics. His espousal of cell theory and insight into the formation and maintenance of tissues resulted in Rudolf Virchow dedicating the English language edition of his ground-breaking book 'Cellular Pathology' to John Goodsir.[3,4]

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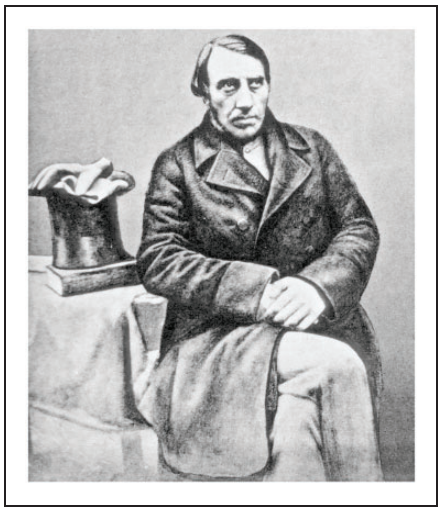

Figure 1. John Goodsir (Public domain image).

Goodsir and *Sarcina ventriculi*

Goodsir seems not to have practised as a physician to any great extent but one clinical paper,[5] published in *The Edinburgh Medical and Surgical Journal* in 1842 and entitled 'History of a case in which a fluid periodically ejected from the stomach contained vegetable organisms (*Sarcina ventriculi*) of an undescribed form', is remarkable for its prescience and attracted the attention of Charles Darwin.

The paper concerns a 19-year-old male who had suffered from a stomach complaint for four months. Every morning the patient vomited a large volume, 'two-thirds to a whole wash-hand basinful', of watery fluid; the regurgitation of such dilute, weakly acidic fluid is often referred to as water brash. The vomitus was described as smelling like fermenting 'worts', i.e. incompletely fermented beer and also vinegar. On standing for a few hours, the vomitus clarified, producing a brown sediment and a 'surface mass of froth like the head of a pot of porter'; the patient had no other symptoms or signs. Given the froth and the smell, Goodsir reasoned that 'this and other cases of similar stomach-complaints might depend on fermentation of the contents of the organ (i.e. the stomach)'.

In keeping with the contemporary theories of fermentation up to this point in the middle of C19 (reviewed in Barnett[6]), Goodsir suggested that fermentation could be chemical or induced by the contents of the stomach, and if the latter were true, as he suspected, then he reasoned that there should be evidence of the fermenting organism in the vomitus or, as he puts it, 'remains of ferment vegetables in the ejected fluid'. Goodsir examined samples of the vomitus under his microscope, finding that every drop that he examined contained tiny organisms 'closely allied to certain genera of BACCILLAREAE and much more closely to the genus GONIUM among the VOLVOCINAE'. This taxonomic classification is long out of date, given that Goodsir was observing a bacterium and bacteria had not even been identified as a taxonomic Kingdom at this time. Goodsir named the organism *Sarcina ventriculi*, believing it to be of vegetable origin (i.e. a plant) and the name is retained today. Goodsir gave the organism the genus name *Sarcina* because of the similarity between the individual organisms to the loculus or satchel within the carrying bundle (*Sarcina*) of a Roman legionnaire[7] (see Figure 2). The modern taxonomy of *Sarcina ventriculi* is that the genus is a Gram-positive coccoid bacterium in the sub-kingdom *Posibacteria*: Phylum *Firmicutes*: Class *Clostridia*: Order Clostridiales: Family Clostridiaceae Taxonomic Serial No. 958067.[10]

S. ventriculi is noted for its ability to survive highly acid environments, indeed its dominant fermentation product is acetic acid.[11] Analysis of the vomitus by Goodsir's colleague Dr George Wilson, described at length in the paper,[5] revealed an 'enormous' quantity of acetic acid in it. The stomach, with its low pH, seems to occasionally provide a favourable niche for the growth of *S. ventriculi*. This is relatively rare, however, and in 2016, the total published clinical literature on *S. ventriculi* comprised 13 cases describing its presence in association with gastric symptoms such as epigastric pain, haematemesis, dyspepsia, dysphagia, diarrhoea, etc.[12] When Goodsir saw these organisms, he immediately considered them 'either as the cause of the symptoms in my patient's case, or at least as very remarkable and important concomitants'.

Therapy

Goodsir prescribed Prussic Acid, in keeping with Granville's monograph on the usage of Prussic Acid in cases of spasms of the stomach,[13] and when this was not effective, Goodsir prescribed creosote. Creosote had long been known to be active against suppuration and putrefaction and was used as a treatment for tuberculosis and pneumonia.[14] Eventually, the principle active component of creosote – carbolic acid – was isolated and used as a topical antiseptic, most notably by Joseph Lister (1827–1912).[14] The course of creosote was a considerable success and in the paper Goodsir declares

> I have it not in my power to state that the complaint is removed, although attacks are much less frequent and the quantity of fluid diminished. The creosote has a most decided control over it and will, I am inclined to believe, ultimately cure it.[5]

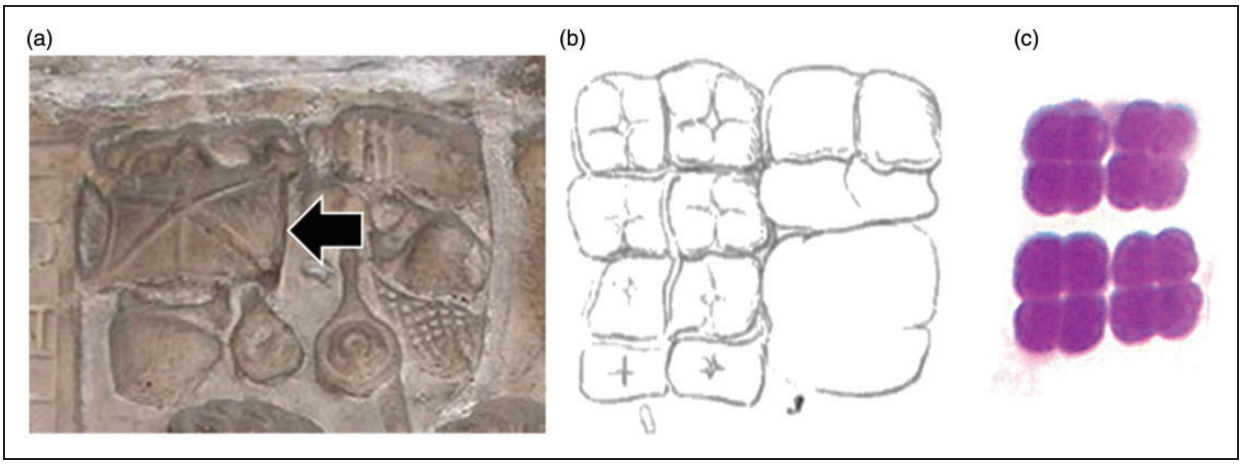

Figure 2. (a) Detail of Trajan's column showing a Roman soldier's *Sarcina* with the loculus at top left (arrow)[7]; (b) Goodsir's drawing of *S. ventriculi* (Plate XI, p. 482 in Vol 2 of Goodsir[8]); (c) Photomicrograph of stained *S. Ventriculi* from Oddó and Diaz[9] (Oddó and Diaz[9] is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.).

In a letter to Charles Darwin, more than 20 years after the publication of this paper,[15] Goodsir appears to confirm this by describing the creosote treatment as a 'complete success' (see later).

Sarcina and Charles Darwin's dyspepsia

The life of Charles Darwin (1809–1882), amongst the most famous scientists of all time, does not need to be elaborated here (Figure 3). His book 'On the Origin of Species by Natural Selection or the Preservation of Favoured Races in the Struggle for Life', based on observations and insights into the natural world garnered during his voyage as ship's naturalist on HMS Beagle from 1831 to 1836 was published in 1859. It shook the foundations of biological science and still resonates profoundly today. On returning from the voyage of the Beagle, Darwin suffered severe and ongoing health problems that plagued him for the rest of his life.[16] The worst of these symptoms have been summarised as 'recurrent nausea, retching and vomiting, gut pain, flatulence, headaches, and a swimming head. He also suffered intermittently from eczema, particularly on the face, also boils and continual fatigue'.[16] Darwin's condition was not diagnosed during his lifetime but efforts to solve the mystery have continued ever since and 31 different causes of Darwin's illness, have been suggested.[16] Although the letter does not appear to survive, Darwin wrote to John Goodsir in the summer of 1863 hoping for a diagnosis of his constant vomiting, as a result of reading Goodsir's paper on *Sarcina*. None of Darwin's letters to Goodsir survive, but the Darwin Correspondence Project contains

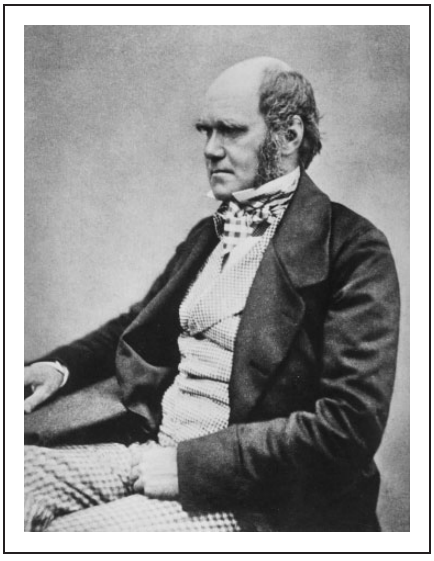

Figure 3. Charles Darwin (Public domain image).

the three letters of reply from Goodsir to Darwin. The correspondence took place four years after the publication of 'On the origin of species by means of natural selection', when Darwin was at the height of his fame. Goodsir, on the other hand, was in ever-poorer health but was still Professor of Anatomy in the University of Edinburgh.[1] In a letter to J.D. Hooker on 25 August 1863,[17] Darwin confirmed that 'I have had a deal of sickness of late; every morning for a fortnight'. As a result, he describes how he has been in communication with 'Professor Goodsir in Edinburgh' informing him of 'vegetable cells in the limpid fluid which I throw up'. Being a microscopist himself, Darwin had apparently

examined some of the vomitus and found 'spherical bodies' which he described in the letter to Goodsir. Goodsir responded to Darwin on 21 August 1863[15] that the 'spherical bodies' were 'probably the cells of Torula, or spores of Penicillium'. Goodsir replied also to what must have been a request from Darwin, that he would 'most willingly examine slides prepared from the vomitus or if not giving you too much trouble, a small quantity of the fluid with the flocculent & tenacious matter sent in a tube or small phial'. Darwin must also have mentioned *Sarcina* in his letter since Goodsir describes *Sarcina*'s unusual morphology to Darwin 'If *Sarcina* be present, it will be at once detected by its square form and peculiar segmentation'. Based on his experience with his own patient, Goodsir recommends

> If your medical adviser has no objection you might try creosote. In the case in which *Sarcina* was first detected, one drop of Creosote was taken at bedtime, and afterwards two drops in the forenoon, and two drops at bedtime with complete success.[15]

In a short letter of 27 August 1863,[18] Goodsir reported on a slide of the vomitus that Darwin had sent him. He reports 'I have obd. (sic) no Sarcinæ on it,' but he did find Torula and crystals of 'biliary matter'. In a further letter dated 28 August 1863, Goodsir reported on a phial of vomitus that he had received from Darwin. In it, he identified the 'alga' Leptothrix, now classified as a bacterium and yeast cells of the Torula species; there is no mention of *Sarcina*. Goodsir did experience problems in fully identifying the organisms in this sample on account of 'putrifactive chang⟨es that⟩ (sic) had taken place' in the sample during its transit from Down House in Kent, where Darwin resided, to Edinburgh. There is no other documented correspondence between Darwin and Goodsir.

Conclusion

Medical (and other) histories have a dominant received narrative, and in microbiology, the linking of a medical condition with a specific micro-organism is almost always allotted to the 'Golden age of bacteriology', approximately 1870–1900.[19–21] In this space of time, the germ theory was fully developed, and an undisputable link demonstrated between infection with a number of specific micro-organisms and specific diseases – see Blevins and Bronze[21] for a list of 20 such diseases, the causative organisms of which were discovered during this 'Golden Age'. Koch's 1876 paper linking *Bacillus anthracis* with anthrax is generally taken to be the first case where a specific bacterium is linked with specific disease.[21,22]

However, Wainwright[23] has questioned this standard account and pointed out that in fact Goodsir, with *Sarcina*, can arguably be considered amongst the first to link a specific micro-organism with a disease, decades before Pasteur and Koch. In addition to Wainwright, several histories of microbiology have recorded Goodsir's early foresight in recognising *Sarcina* and its link to the vomiting disorder.[20,22,24] Goodsir, however, was not a microbiologist and did not take any of the technical steps in use by Koch's time, such as deriving pure cultures or the execution of Koch's postulates to confirm the link. At that point in time, there were no ground-rules to follow for a science of microbiology, so implicating a micro-organism with a specific disease rested solely on visualisation by microscopy in a lesion or in the fluids of an afflicted patient i.e. correlation. Thus, the potential for the classical error of confusing correlation with causation can be levelled at Goodsir's *Sarcina* paper. Certainly, *Sarcina* is found in humans with no associated disease, as stated recently – 'Review of the published cases along with our case suggests that it is more frequently an innocent bystander rather than a pathogenic organism'.[25] On the other hand, *S. ventriculi* can occasionally be associated with a severe, even fatal stomach pathology – emphysematous gastritis.[26] Therefore, there are three different manifestations of *S. ventriculi*'s association with the stomach:- commensal, fermentation with water-brash and invader of the interstitium of the gastric wall to cause emphysematous gastritis. Of these, only the water brash manifestation was apparent in Goodsir's patient, and so his observations on *Sarcina* are limited and not to be overstated. They do, however, show pathobiological insight, occurring as they did in the early 1840s, decades before the 'Golden Age of Bacteriology'. Other instances of individuals having insight into infection has led Wainwright to conclude that 'Clearly microbiologists (i.e. pathologists), working well before Pasteur, used microscopes to observe bacteria and fungi and concluded that such organisms could cause diseases in humans. Some even attempted to cure such infections using chemicals.'[27] In that regard, Goodsir recommended internal treatment with an antiseptic – creosote – and reported it to be curative in this single case.

Goodsir's prescience in cell theory and cellular pathology was recognised by none other than Virchow himself,[3] and Goodsir's paper on *Sarcina* demonstrates that his foresight extended to the microbiological world and its link to disease. Lonsdale[1] notes that Goodsir's occupation of the Chair of Anatomy at

Edinburgh University in 1843, led him to focus thereafter on teaching at the expense of research and publication. This may have robbed the world of further remarkable advances and early insights in other topics on which the searching and brilliant mind of John Goodsir might have alighted.

Charles Darwin, perhaps the greatest and most influential figure in the history of biology, contacted Goodsir having read the *Sarcina* paper. He sought to determine whether his own daily vomiting, mimicking the individual in the *Sarcina* paper, might also be due to *Sarcina*. Infection with *Sarcina* was not the seat of Darwin's problem, as Goodsir confirmed from his examination of Darwin's vomitus and Darwin went on suffering serious ill health for another 20 years up until his death in 1882.[16] Recently, it has been persuasively argued that Darwin suffered from lactose intolerance at a time when such a condition was totally unknown,[16] and therefore no intervention could be made. Records of Down House show that the household had a high dairy content in their diet, which was typical for the time,[16] and Darwin's symptoms are strikingly in accordance with those of someone who is lactose intolerant. In the current era, where lactose intolerance is understood, there is no treatment, but the simple intervention of eliminating dairy products from the diet essentially avoids the symptoms.

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