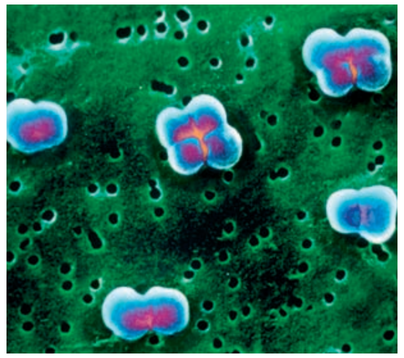
The fossil hunter, Queen Victoria's doctor and the germ theory of disease

Before the development of the germ theory, people generally believed that infections were caused by the spread of bad air or 'miasma'. **Milton Wainwright** shows that as early as the 1840s there were speculations that microscopic organisms might be responsible for disease.

Prior to the work of Louis Pasteur, most scientists believed that diseases were spread by poisonous gases or bad air, so called miasma. However, while the miasma theory was dominant in the early 1800s, some scientists came to the conclusion that disease can be caused, and spread, by microscopic organisms, or animalculae. During the 1840–1850s in particular, considerable progress was made in refining this view. At the forefront of this work was the Scottish pathologist, **Sir John Goodsir**. In the early 1840s, he was interested in a stomach disease in which a fermenting, wort-like ejection was produced. On examining the ejections under the microscope Goodsir found a vegetable organism made up of small cells occurring in packets of four, which he named *Sarcina ventriculi*. Having realized what was causing the disease, Goodsir then set about eradicating *Sarcina* by giving the patients oral hyposulfites. As a result, by 1842, a bacterium had been recognized, named and linked directly to the cause of a disease, leading to successful attempts to destroy the organism and thereby affect a cure.



▲ Left. John Goodsir (1814–1867). Engraving. *Wellcome Library, London*

▲ Right. Portrait of Dr Gideon Algernon Mantell (1790–1852), British geologist/ palaeontologist and country doctor. *Geological Society / NHMPL*

◀ Left. Coloured scanning electron micrograph of *Sarcina* sp. bacteria, originally discovered and named by Sir John Goodsir. *BSIP / Science Photo Library*

◀ Right. Original iguanodon teeth as found by Annie Mantell and described by her husband. *Natural History Museum, London*

The presence of minute organisms in vomit was confirmed by a certain Dr Goodfellow in 1844, who also found them in both blood and faeces. He noted that the organisms were very similar to those found in stagnant waters and suggested that, because of their minute size, they could pass from the blood into the stomach. Both Goodsir and Goodfellow seem to have been content to report these single incidences and they failed to extrapolate their findings to formulate a general germ theory. Two other medical luminaries did, however, manage to develop germ theories a decade or more before Pasteur began his studies.

The fossil hunter and the germ

In the early 1800s, increasing numbers of fossilized animals were being discovered. At the forefront of this research were **Gideon Algernon Mantell**, a physician in the Sussex town of Lewes, and his wife Annie. Mantell is best known for his discovery of the iguanodon, but he was also a keen microscopist, particularly interested in animalcules. In 1846, Mantell wrote *Thoughts on Animalcules: or a Glimpse of the Invisible World Revealed by the Microscope*, which although mainly devoted to studies of pond water, also includes a reference to the germ theory:

> *'It is probable that many of the most serious maladies which afflict humanity are produced by peculiar states of invisible animalcular life. From some periodical and exaggerated conditions of development, particular species, too minute for the most powerful microscopes to descry, may suddenly swarm in the air, or in the waters, and penetrating the internal vessels and organs, exert an injurious influence of a specific character, on the linings and fluids of the human frame. And from this inscrutable agency, may, possibly, originate the cholera, influenza, and other epidemic disease.'*

An anonymous reviewer in the *Lancet* dismissed Mantell's views:

> *'It must be acknowledged that the mays and the possibilities are very convenient items in medical hypotheses … Our readers must not assign too high a value to these speculations.'*

Mantell was obviously convinced that diseases were caused by very small animalcules, (but importantly, not 'animals' such as *Hydra* and *Paramecium*) and concluded that such small forms were spread in the air and water, and caused specific disease. Mantell also observed bacteria which he called *Vibrio*, or 'trembling animalcules', and suggested that mercury could be used to kill such infective agents, which he believed caused diseases like erysipelas.

Queen Victoria's doctor and the germ

One of the most impressive early contributions to the germ theory was made by Sir Henry Holland, Queen Victoria's physician, a well known socialite and world traveller. An active member of the Royal Institution, Holland knew most of the great scientists of the day. He was also a cousin and friend of Charles Darwin. In his *Medical Notes and Reflections* (1839) he discusses his views on the cause of cholera:

> '*We may look to animalcule life, diffused by the atmosphere, or by man as the source of the disease, in a form not recognizable by our senses, or other direct means of research, but nevertheless subject to some similar laws of propagation and diffusion as species more obvious to us and producing virus which acts noxiously on the human body.*'

Holland, who was clearly influenced by Mantell's book, also noted that cholera appeared to spread along water-courses. By 1855, his own book had reached its third edition and his views on the animalcular nature of human disease, notably cholera, were much extended. In the first edition he referred to 'insects' as the causal agent of disease but it is important to note that this term was often used as a synonym for animalculae. By the third edition Holland was using animalculae instead. He began this edition by claiming priority on the view that animalcules cause disease, dating back to 1839. Even then, he admitted that his ideas were not entirely novel and that similar speculations had been made as early as the 1700s.

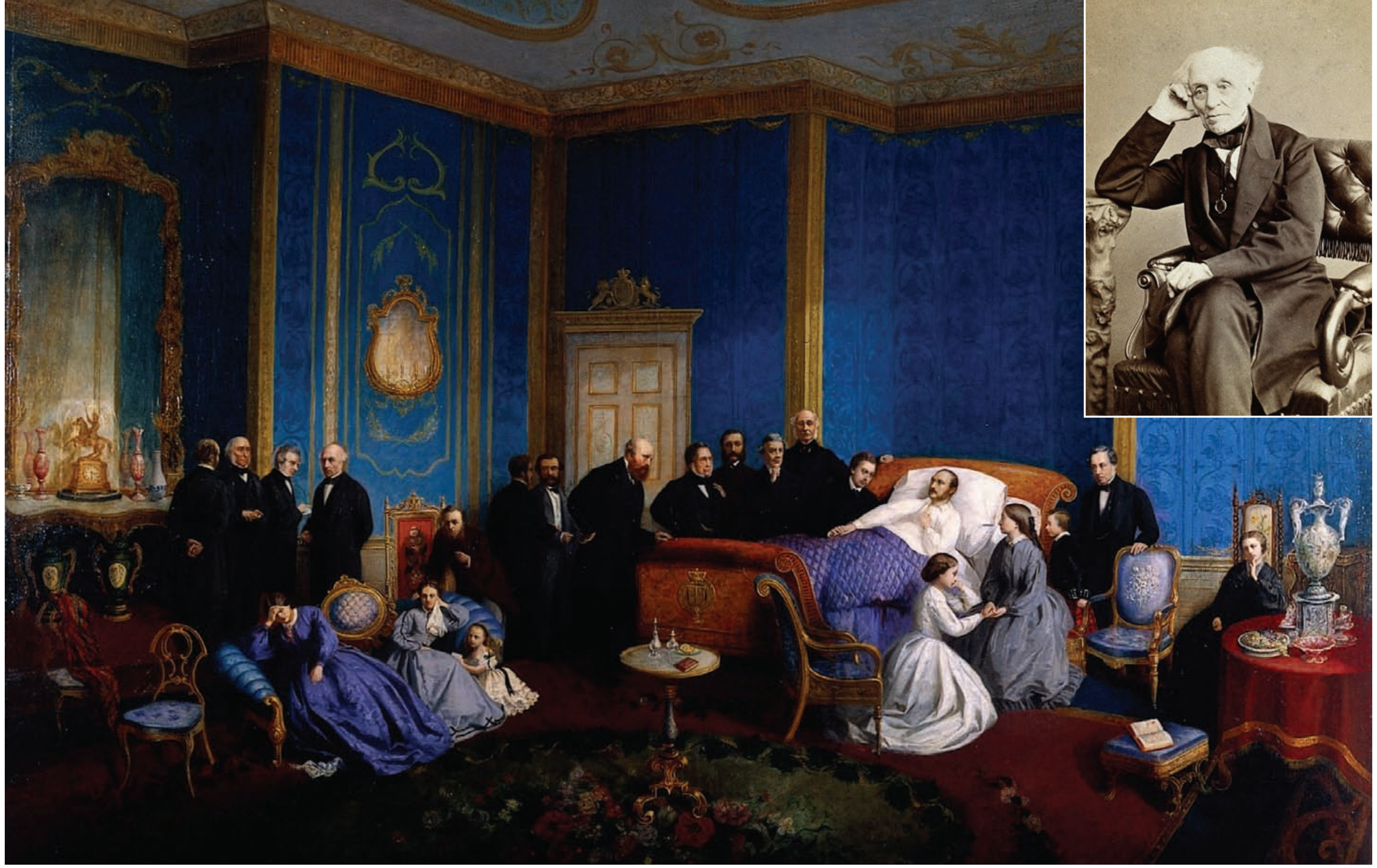
Holland asserted that animalcules were spread in the atmosphere and could '*act as a noxious or poisonous influence on the human body*', and that '*when* applied (my emphasis) *to the absorbing surface of the body they may produce the most virulent symptoms of disorder, locally or generally, according to the nature of the virus and its intensity*'. (The term virus was often used during this period to mean an infective agent, rather than in its modern sense.) This is a remarkable statement, since it suggests that he was aware of experiments where infective material, containing animalculae, had been used to induce disease.

Holland devoted much of his book to cholera, being much against the view that electrical and chemical phenomena were responsible. Instead, he regarded it as being a '*material poison which is specific in its effects and is capable of reproducing itself and propagating over the globe*'. Significantly, Holland dismissed the then common view that cholera was caused by fungi (which he called vegetable life), but instead implicated animalcules (which he deemed to be animal life). He also noted that germs often remained dormant for long and indefinite periods, yet like seeds '*burst into active existence when the circumstances occur to favour a change*'. He argued against the view that life (in simple forms) cannot arise spontaneously, but instead he stood by the 'old dogma', '*Omne vivum ab ovo*'.

Holland also believed that diseases such as smallpox and syphilis appear and disappear, not so much because the agent alters, but because '*the physical constitution of races and communities of men seems in time to habituate itself to certain morbid agents and conditions of disease*'. Holland also claimed that the cause of diseases such as the Black Death and cholera may have some '*certain common relation*', but that the virus of the disease is '*doubtless not identical*'.

Holland made one fundamental error in believing that cholera was not conveyed '*through drinking water, or food, which has alas been contaminated by the evacuations or other contact with patients under the disease*'. Why did he conclude that cholera was not water-borne, especially when he believed that watercourses somehow provided a means of spreading it? The answer can be found in 1835 when he studied an outbreak of cholera in Trollhattan, a Swedish village of scattered dwellings supplied with water from Lake Wenern, described as being '*as clear as a mountain spring*'. Cholera suddenly appeared in this seemingly pristine place and killed 48 people, about a tenth of the population. It was this paradoxical situation that induced Holland, somewhat reasonably, to conclude that cholera was not a water-borne disease.

Holland ended his book by stating that viruses (i.e. germs) cause disease by their ability to produce specific poisons, which explains why some people, but not others, succumb. Finally, he suggested that at some future point diseases like cholera will be cured by the finding of '*a specific antidote to the action of the virus on the blood*'. Although he was using cholera as an example, he was confident that his hypothesis extended to other infectious diseases.



▲ The last moments of HRH the Prince Consort in 1861 captured in an oil painting by Oakley under the pseudonym Le Port. Sir Henry Holland (1788–1873), Queen Victoria's physician, is depicted standing with a group of physicians on the left of the picture. *Wellcome Library, London*

▲ Inset. Sir Henry Holland photographed in 1867 by Ernest Edwards. *Wellcome Library, London*

Other views

Other scientists working in the 1840s were clearly aware of the role of bacteria in disease. In 1848, for example, the English physician, Thomas Henry Starr published *A Discourse on the Asiatic Cholera* in which he opined:

> '*I am inclined to favour the somewhat obsolete doctrine which teaches that such visitations are due to animalcular sources. These germs are too subtle for us to penetrate the mysteries of their existence, even with the highest microscopical aid.*'

He then went on to draw analogies with the diseases of the vegetable world which 'depend on animalcular visitation, and that the decomposition depends on the same as does the formation of many geological structures'.

Contrary to popular belief then, much was known about the role of microscopic organisms in disease during the 1840s, a decade or more before Pasteur began his work. Hopefully, the unsung contributions of men like Mantell and Holland to discovering the role that micro-organisms play in disease will, at last, become fully recognized.

Milton Wainwright
Department of Molecular Biology and Biotechnology, University of Sheffield, Sheffield S10 2TN, UK
(e m.wainwright@sheffield.ac.uk)

Further reading

Anon. (1846). Review of Mantell's *Thoughts on Animalcules*. *Lancet* ii, 478–479.

Holland, S. (1839). *Medical Notes and Reflections*. London: Longmans.

Mantell, G.A. (1846). *Thoughts on Animalcules; or a Glimpse of the Invisible World Revealed by the Microscope*. London: Murray.

Spokes, S. (1927). *Gideon Algernon Mantell*. London: Bale and Danielsson.

Starr, T.H. (1848). *A Discourse on the Asiatic Cholera*. London: Churchill.

Wainwright, M. (2003). An alternative view of the early history of microbiology. *Adv Appl Microbiol* 52, 333–353.