INFLAMMATION, SUPPURATION, PUTREFACTION, FERMENTATION: JOSEPH LISTER’S MICROBIOLOGY

by

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This paper focuses on Lister’s inaugural lecture at King’s College, London, in October 1877. As the new Professor of Clinical Surgery, Lister had much to report, including impressively high survival rates from complex operations previously regarded as foolhardy. Instead, he chose to address the processes of fermentation in wine, blood and milk. His reasons are not obvious to a modern audience, just as they probably were not to those who heard him in the Great Hall at King’s. Having brought microbiological apparatus from his laboratory to the lecture theatre and presented proof of bacterial variety and specificity, Lister publicly demonstrated the creation of the first pure bacterial culture in the history of microbiology. It was an ingenious and well-thought-out strategy designed to generate a frame of mind among his new colleagues and future students, receptive to the causative role of bacteria in septic diseases. His timing was impeccable.

Keywords: lactic acid bacteria; pure bacterial culture; germ theory; fermentation; infection transmission

INTRODUCTION

Recent discussions of Lister’s microbiology focus on a paper he delivered just before Christmas 1877 at the Pathological Society of London, and published in their Transactions in 1878: a paper reprinted and discussed on several occasions in the previous 50 years. Lister presented essentially the same findings twice. The focus here is the Pathological Society paper’s antecedent twin, hitherto insufficiently noticed.

Lister’s introductory address for the opening of the medical school year was delivered at King’s College, London, on 1 October 1877. After more than two decades in Scotland, where he had developed his theory and practice of antisepsis, the event marked Lister’s return to London to take up a new chair in Clinical Surgery. Lister’s address, delivered nearly three months ahead of his appearance at the Pathological Society of London, was also his own inaugural lecture.

Three versions of this landmark address at King’s College survive. The British Medical Journal published an extensive transcript within a week, and Lister subsequently published a
corrected version of the text in the Quarterly Journal of Microscopical Science. Among Lister’s scientific papers the original transcript of Lister’s address survives, taken down by a shorthand writer as it was delivered in King’s Great Hall and rendered into good legible longhand.

The shorthand writer from Messrs Walsh & Sons of Parliament Street floundered occasionally with scientific terms, and left gaps to be duly filled in later, but the transcript has exciting immediacy and possesses details lacking from the printed versions. At one point, Lister became aware of restiveness in his audience—probably among students who had little conception of what they were actually witnessing—and asked for forbearance:

I am sorry that anything I should say should seem in any way wearisome to any gentleman here... if it is so, I would only beg him for the sake of others who seem to have some interest in what is going on, to refrain from giving evidence of his weariness.

The published versions lack any sign of this. From it we can deduce the breadth of the audience for this lecture: not just college and Royal Society luminaries, but also perhaps some people with no real idea who Lister was, and others expecting a clinical lecture from a great clinician, who could not fathom why the new Professor of Clinical Surgery should be intent upon telling them about fermenting liquids, putrefaction, and milking cows.

In the transcript, too, none of the applause has been edited out. References to it are struck through with emphatic zigzag or scrambling deletions, but reading behind them reveals that Lister had considerable support in the hall. He was applauded repeatedly from the outset, when he reported pondering whether to do the traditional thing and address the beneficent calling to which students were devoting themselves, or attempt some special subject, ‘in the hope that I might say something which may have interest, and if possible even instruction not only for the student but also for the eminent men whom I have the honour to see around me.’

Lister chose to take this latter course, and a substantial piece of work it was. The lecture was packed with data from laboratory researches conducted with his wife, Agnes, with increasing refinement, over several years. The previous two months, since leaving his post in Edinburgh, had seen the culmination of this work.

King’s College

The new professorship at King’s College was a significant moment for Lister. Personally, it meant that he had to leave Scotland where he had lived and worked for years, and his wife’s home town of Edinburgh, to move back closer to his own London roots. Professionally, it set him on a course that his younger acolytes seem to have regarded as a crusade to persuade the recalcitrant metropolitan surgical establishment to adopt antisepsis.

Lister was 51 years old, with a brilliant career behind him: Regius Professor of Surgery at Glasgow, Professor of Clinical Surgery at Edinburgh, Fellow of the Royal Society. He had been a controversial figure in British surgery for at least a decade, especially since The Lancet’s publication in 1867 of Lister’s high-profile series on his new antiseptic treatment for compound fractures, potentially mortal injuries. His ideas had been implemented with excellent results in various places in the UK and abroad, and in 1871 Lister had been chosen to operate on Queen Victoria, a sure sign that in high places his work was recognized and
Lister had been exercised by the unpredictability of patient outcomes after surgery since his student days. However dextrous a surgical operation might be, wound infections carried off many patients. The navigation of hope and fear in the days after an operation was difficult for patient and doctor alike. Someone of Lister’s earnest temperament could not fail to be affected by the tragically high mortality of patients in hospital wards, and the sheer relief of unexpected recoveries. Early training under his microscopist father meant that Lister was highly sensitive to the teeming life of the very small. His intellectual life as a doctor was characterized by a growing preoccupation with inflammation, suppuration, putrefaction and fermentation.

THE YEAR 1877 IN CONTEXT

‘Fermentation’ was the term Lister used for the putrefactive process of sepsis that we might now describe as wound infection. Discussions of Lister’s work often start with his exposure in the mid 1860s to Pasteur’s discovery of the biological causes of fermentation itself. There had long been debate in the UK about the causes and spread of disease. Microscopic evidence of waterborne organisms had been widely available since the 1820s, when a famous caricature featured one of the famed shows of London: an oxy-hydrogen microscope that projected the contents of a drop of London water to 14 feet across. Lister himself was evidently looking for the microscopic causes of infective processes in erysipelas and ‘hospital gangrene’ when he was a medical student in the 1850s. By the mid 1860s Liebig’s solely chemical explanations of the physical changes wrought by fermentation were giving way to Pasteur’s proofs that such processes were engendered by living entities. But until the mid 1870s there remained uncertainty as to whether these entities were plant-derived or animal-derived, and how they spread. Controversy surrounded whether they were generated spontaneously or needed seeds or ‘germs’, and if they were genuinely causative of diseases or simply existed harmlessly alongside them, and whether or not particles of a ferment could be transmitted.

Intelligent medical men took vigorous positions on both sides, but for a long time progress was inching, and ignorance profound. The puzzle was beginning to receive intelligent scrutiny, however, and the search was on for proofs of the real nature of these organisms and perhaps for the specific causes of specific diseases.

By the mid 1870s several indications had emerged to suggest that some veterinary and human diseases might be caused by invasions of ‘low’ forms of life, and Lister certainly knew that surgical instruments might serve as a means of transmission. In Prussia, Ferdinand Cohn was developing a taxonomy of microscopic organisms and had named several bacterial forms, doubly helpful to other researchers by allowing them to make sense of what they were seeing and fostering a pan-European language for this new conversation.

Between 1875 and 1877 the journals seem full of energetic argument between supporters of spontaneous generation and of ‘contagium vivum’, and a growing sense that the debate was nearing a conclusion. In his 1876 address to the Royal Microscopical Society, the President, H. C. Sorby, discussed the problem of ‘the limit of the powers of the
microscope and the ultimate molecules of matter’ and the ‘Theory of Invisible Germs’. The problem was in part a difficulty of visualization, of the nature of light and of existing lenses. Even the most powerful modern microscopes, Sorby said, were incapable of detecting the really small, which meant an ‘almost endless variety’ of germs of living matter might exist, ‘each having a distinct structural character, and yet each so small that there is no probability of our ever being able to see them, even as indefinite points.’

When John Tyndall took up ‘the floating matter of the air’, also in 1876, he brilliantly confirmed Pasteur’s demolition of prevailing arguments in favour of spontaneous generation, by demonstrating to packed audiences at London’s Royal Institution that aerial dust might carry living particles. ‘As far as experimental enquiry has hitherto penetrated’, Tyndall announced, ‘life has never been proved to appear independently of antecedent life.’

The Quarterly Journal of Microscopical Science carried two important essays by Francis Bell within months: the first (July 1876) on Cohn’s recent work exposing the organism responsible for persisting beliefs in spontaneous generation to be a heat-resistant anaerobe recalcitrant to eradication, already named \textit{Bacillus subtilis} by Pasteur. Then in January 1877 Bell comprehensively reviewed Koch’s first data on splenic fever, a veterinary disease contagious to humans, caused by a large organism already described by Davaine and now known as anthrax. Koch had worked alone, using live animals (mice, rabbits and guinea-pigs) to trace the organism’s life cycle.

During the summer of 1877 Lister was working with Agnes in his Edinburgh laboratory, while in Manchester, at the British Medical Association summer meeting, William Roberts (Physician to the Manchester Royal Infirmary, Professor of Clinical Medicine at Owens College) delivered an address on ‘The Doctrine of Contagium Vivum and its Applications to Medicine’. Roberts recognized that Lister’s application of germ theory to the antiseptic care of wounds had made the subject ‘of universal interest to medical practitioners’. A seasoned bacteriological investigator himself, Roberts praised Koch’s first published work and went on to offer his medical audience two memorable ideas. First, having closely monitored the process of fermentation after the addition of yeast to a bottle of urine, Roberts compared the incubation, disturbance, rise in temperature, and subsidence of the ferment in the urine with the profile of a contagious fever such as smallpox in the human body, described what he had seen as a ‘fever in a bottle’, a powerfully imaginative analogy that many present could visualize and understand, despite not having witnessed the experiment. The human body had long been conceived as a vessel; now it could be perceived as constituting a growth medium. Disease bacteria—’germinal particles’—might better be conceptualized as living parasites than as inanimate ferments, Roberts urged, and infective transmissibility must be recognized. Depending on his fellow doctors’ practical understanding of fevers and of parasites, and to help them categorize what then was stirring in the world of microscopy, Roberts foresaw that if the doctrine of ‘contagium vivum’ be ‘firmly grasped by capable hands’, it would ‘prove a powerful instrument of future discoveries.’

\textbf{The topicality of Lister’s lecture}

Lister knew Tyndall and Roberts and their work, and had probably read Francis Bell with interest. His ideas about the fatal development of sepsis in the body had developed apace...
since his introduction in 1865 (by a faculty colleague in chemistry at Glasgow) to Pasteur’s work on fermentation. Since then, in parallel with his daily clinical work, Lister had been conducting careful laboratory-to-clinic experiments on the prevention of sepsis in wounds and surgical incisions, and had published a string of important papers. However, for his inaugural lecture in 1877 Lister chose not to look back over his published successes in using carbolic in surgical operations, his successful treatment of open wounds, abscesses and compound fractures, his specially treated ligatures, antiseptic dressings, or the remarkable statistics emerging at home and abroad concerning new and successful antiseptic operations that had previously been regarded as foolhardy or murderous. As the new Professor of Clinical Surgery at King’s College, Lister could pertinently have addressed any or all of these clinical topics. Instead he chose to present his work on the nature of fermentation in the context of three key fluids: wine, blood and milk.

Ahead of his move to London, Lister had made the decision to revisit his own experimental work on organisms involved in fermentation, a study in which he had been deeply engaged at intervals since at least 1873. Now, during work on the materials that he would present at his inaugural lecture at King’s College, Lister at last saw how to perfect his earlier experiments.

The audience in the Great Hall at King’s was invited to join him in a process of investigation rooted in the knowledge that surgery and childbirth were often followed by terrible deaths of unknown cause. Lister’s story was simply told, in language that allowed everyone to follow his reasoning and to understand the refinements of thought and technique along his path of discovery. His lecture involved the audience in a narrative, elucidating the course of a painstaking and persistent effort—involving puzzlement, experiment, false starts and failures, meticulous experimentation, logical inference, statistical analysis and dawning understanding—towards new and valuable knowledge.

**Lister’s Commonplace Books**

Much can be learned about Lister’s private studies because he left behind some enormous leather-bound volumes of scientific notes: his Commonplace Books. Beautifully rebound after his death, they are kept safely in the Archives of the Royal College of Surgeons of London. They are full, margin-to-margin with notes, not indexed, strangely, and also curiously poorly organized internally. They are a personal record of Lister’s work process, undertaken at his own pace, recorded for his own use. Accessing these notebooks with any facility was probably dependent on memory. We know from his nephew Rickman Godlee’s fine biography that Lister often left lecture-writing until the last minute, in ‘desperate haste, which even on the most important occasions, he seemed unable to avoid.’ Lister seems to have preferred dictation, which is fortunate for us because his wife’s handwriting is much more easily decipherable than his own.

Blank areas were left in the text in many places, and small drawings carefully glued in, showing what Lister had seen down his microscope. Each is briefly dated and scaled so as to be inserted correctly in the notebooks, a labour that I suspect also fell to Agnes. The images demonstrate the laboriousness of the process of observation, and at what magnifications Lister was able to work: drawing the smallest visible structures in as much detail as he could at the limits of the technology of the day. His meticulous assiduity
allows an understanding of the extent to which—alongside his clinical responsibilities as a pioneering surgeon and a key figure in great institutions—Lister was also a committed and indefatigable scientist.

Lister’s Commonplace Books span the years 1870–99, during which he developed his own scientific method, by trial and error, making his own transition—along with a small number of other individuals of his cohort, and with advice in 1874 from Pasteur—from concerned surgeon and microscopist to pioneering bacteriologist. To understand his achievement we have to forget oil-immersion lenses, electron microscopy and even secondary-school science laboratories. Lister used test tubes and owned at least one Bunsen burner, but he worked out his own mode of sterilization using prolonged heat in a ‘hot-box’ (an autoclave of his own devising), built his own apparatus, designed a bespoke micropipette, and devised systems of air filtration and kit for manipulating sterilized (he called it ‘heated’ or ‘roasted’) equipment. For bacterial cultures Lister used domestic liqueur glasses, and what he called a ‘glass garden’, all this work being accomplished before the invention of the Petri dish.

**LIVING FERMENTS**

Lister began his important address by explaining fundamentals: he was considering fermentation because sepsis and puerperal fever were thought likely to be caused by ferments; the subject was an important one not only for surgeons but also for physicians and accoucheurs. Lister mentioned having just returned from the wine harvest in Italy, where he had been told of the vats ‘boiling over’ during the fermentation process. The action of yeast in wine-making was undisputed, he said, flagging up Pasteur’s finding that yeast lived on the grape’s skin. In wine-making, fermentation did not start until the fruit’s skin had been breached. Fermentation is not a chemical reaction, Lister emphasized, but a living process.

Applause broke out in the hall when Lister said he would be addressing the idea that self-multiplying organisms were ‘concomitants’ of the ferment—that they were mere associates or unimportant attendants in the process of fermentation. Lister spoke with restraint towards those ‘high authorities’ who still maintained such a view, saying firmly: ‘it is our duty if we can to disprove it’. Lister made no mention of the shock that he and his team had experienced on entering the reeking wards at King’s College Hospital. He simply presented instead these blood samples uncorrupted after six weeks, which probably surprised most of the medical men in the hall, all of whom would have felt the importance of the demonstration even if they were mystified by its mechanism.
The same specimens demonstrated the fallacious notion that it was oxygen that caused blood to putrefy. Lister stated, however, that if a tiny amount of putrefied blood ‘say, on the end of a needle’ were to be added to this uncorrupted blood, its entire mass would soon be affected by ‘putrefactive fermentation’. Those in the hall, or subsequently reading this lecture in print, would of course be aware that mortal wounds—‘needlestick’ injuries now—were an occupational hazard of the dissection room, the operating theatre, the surgical ward and the post-mortem room. Apparently inconsequential wounds (sometimes a mere accidental scratch) had killed many a promising medical man. Lister made no explicit mention of this common professional knowledge but left the idea hanging with his reference to the needle laced with putrefaction; he went on to describe the rod-like bacteria—with remarkable powers of locomotion—that he had found developing in correlation (‘pari-passu’) with the process of putrefaction in ox blood.

Lister pondered why anyone should doubt the relationship between bacteria and putrefaction when the analogy with yeast was so clear. How could anyone think that bacteria might be ‘accidental concomitants’? A large poster (figure 1) demonstrated the enormity of Pasteur’s yeast organism relative to these far smaller bacteria, so that Lister’s audience might appreciate the intellectual difficulty in attributing significant effects to objects so small, and the problem of finding them.

Figure 1. Hand-painted poster used at Lister’s inaugural lecture at King’s College London. The lowest yeast globule is 22 cm long, the individual lactis segments at top right are 3.5 cm. See note 33. (Image reproduced by courtesy of the Royal College of Surgeons of England.) (Online version in colour.)

Lister’s microbiology
Lister then showed a glass of a ‘highly putrescible’ mixture—mixed fresh blood and sterile water—that, having been protected from aerial dust, was still brilliantly clear after an entire month. Manifestly neither oxygen nor moisture caused putrefaction in blood, he concluded. Lister felt it essential to show these uncorrupted specimens physically in their bottles. Unlike William Roberts, his appeal was less to the imaginations of those present than to their faculties of observation and logic. Lister invited his audience to witness the validity of his experimental proofs by direct demonstration.

Fermentation in milk was Lister’s next consideration. He chose this familiar fluid, he said, because ‘it seemed more convenient for the purpose’, but Godlee provides a further convincing reason for Lister’s choice: ‘Milk is the most difficult of all animal fluids to deal with. Supplying nutriment in a form which is acceptable to nearly every germ that infests air and water, it can scarcely be obtained uncontaminated. . . Milk was the last hope of the believers in spontaneous generation.’ Lister described the usual process of coagulation, souring and decay, and mentioned that Louis Pasteur had seen organisms in souring milk that, Lister said, under the microscope were evidently bacteria. Lister had designated the particular organism involved ‘Bacterium lactis’, and he described its characteristics: motionless oval rods which multiplied by division ‘transverse to the vertical axis’, always to be found when lactic acid souring was occurring in milk. Lister laid considerable emphasis on bacterial variety: although this particular bacterium thrived in milk, it scantily survived but did not thrive in Pasteur’s special nutrient solution, which suggested to Lister that bacteria have their own favoured media.

Among Lister’s audience some were doubtless aware that lactic acid was known to be a by-product of putrefaction in the human body. Lister did not raise the matter. Nor did he mention therapeutic trials recently reported in The Lancet concerning the use of milk as a substitute for blood in transfusions after heavy blood loss.

There followed the outline of a process of experimentation on milk—including temporary setbacks and contaminations—demonstrating that souring is not an inherent quality of milk itself, but the work of this specific and separable bacterium. A flask of boiled milk, protected from aerial dust, still liquid and sweet after more than a month, demonstrated that—contrary to existing theories—neither caseine nor oxygen could be held responsible for milk fermentation, because both were present in the unfermented liquid. Fermentation requires ‘something to be introduced from without’. If a series of receptacles of such liquid milk were to be injected each with a drop of ordinary water, a variety of organisms would grow, Lister explained, but not Bacterium lactis. A similar thing would occur if milk in another series of receptacles were to be exposed for half an hour to the air at different locations. Both water and air carried a diversity of organisms, most of which Lister said—unobtrusively opening up the field to his younger audience—were as yet undescribed in the scientific literature. The diversity of organisms growing in the exposed milk allowed Lister to infer that Bacterium lactis was comparatively rare in nature. But he asserted that a needle’s point of souring milk would convert the entire mass of his sweet milk to ‘a sour clot’ within two or three days.

Some contemporaries, Lister recognized, might argue that milk was changed in some way by boiling: that fresh milk might contain ‘certain chemical substances prone to evolve into organisms by spontaneous generation’. To test whether fresh milk naturally contained the organisms that caused its own fermentation, Lister had devised a special manner of collection, just as he had with the ox blood. He found that milk collected in the cow house would stay fresher for longer than milk collected in the dairy, from which he
concluded that *Bacterium lactis* was ubiquitous in the dairy. His first experiment that summer had been on fresh milk collected in a cow house: it was free of *Bacterium lactis* but teemed with other bacterial life. His second attempt—on a fine day in the open air—also showed no *Bacterium lactis* but developed a glorious assortment of growths including ‘strange scarlet spots’, green, brown and yellow blotches and layers, and the most delicate fungal filaments he had ever seen. Here, another hand-painted poster (figure 2) demonstrated the variety of coloured growths produced.38

‘How are we to explain these strange appearances?’ Lister pondered, and went on to answer: had the *Bacterium lactis* been present, it would have colonized the milk and in its development would have taken precedence over all other organisms. The chemical changes it engendered—lactic acidification—would have rendered the milk inhospitable to other organisms.

For his final experimental series, Lister had requested the dairywoman to wash her hands and to cleanse the cow’s udder with new milk. Only then had the milk been squirted into heat-treated glasses directly from the cow, out in the open air of a country orchard near the village of Corstorphine, west of Edinburgh, six weeks previously (figures 3 and 4).39 The morning had been drizzly and Lister had hoped the air had been rinsed clean. The specimens of Corstophine milk had been carried with extreme care to London, and all 12 glasses now stood before his audience. Lister described their appearance as white and apparently pure, yet in reality, he said, ten of them had shown signs of bacterial
Figure 3. A drawing from one of Lister’s Commonplace Books, showing a cluster of test tubes used in his lactis experiments. See note 39. (Reproduced by courtesy of the Royal College of Surgeons of England.)

Figure 4. A cluster of test tubes in the Lister Collection at the Science Museum, London. (Photograph courtesy of the Science Museum, London/Wellcome Library (L0058562).) (Online version in colour.)
development in the weeks since the milk had been collected that fresh Edinburgh morning in the fields. The remaining two, however, were pure, sweet and perfectly fluid. They showed the same litmus reaction as that of fresh milk, and under the microscope they yielded sight of no organisms at all. Lister felt confident enough from this experiment to conclude that fresh milk is not inherently fermentative.

It was at this point that the restiveness among the audience (mentioned above) became apparent, and Lister asked for attention for the more important part of his lecture, which was to 'find absolute evidence, if possible' whether \textit{Bacterium lactis} was or was not the cause of lactic acid fermentation. To decide this point, he had devised a new experiment to obtain a pure culture of \textit{Bacterium lactis}. Lister calculated the numbers of this bacterium existing in a specific volume of milk by actually counting how many individual bacteria appeared in a series of optical fields under his microscope, each field accommodating one-fiftieth of a minim. Numerous such reckonings may be found from that summer in his Commonplace Books. By taking an average, he then calculated that if the milk were to be diluted with a million parts of boiled water, ‘rather less than one bacterium’ would be found on average in every drop. Uniform single drops of this watery milk were dropped (from a micropipette of Lister’s own devising (figure 5)) into each of five glasses of the pure milk. His calculations proved correct: four did not curdle and did not ferment. The dilution of the drop having been done with reference to the incidence of \textit{Bacterium lactis}, they did not grow other bacteria either. The single glass that curdled ‘had the \textit{Bacterium lactis} in abundance’.

Figure 5. The micropipette that Lister designed and had specially made for his lactis experiments. (Photograph courtesy of the Science Museum, London/Wellcome Library (L0057826).) (Online version in colour.)
From this pure bacterial culture, Lister undertook a final experiment: to test it by using it as the basis for a fresh culture by dilution. This time ten glasses were used, some to receive an average of one bacterium per drop, others two, and another four. The one with four bacteria per drop curdled soonest, followed by others with two, and some with one. All remained pure white. Five of the samples had remained fluid, implying, he said, ‘that the particles of the ferment were not uniformly distributed’. The cause of the ferment must be particulate, Lister stressed: it could not be in solution, or the curdling would have occurred evenly throughout all the glasses. Each of the glasses that had curdled had been confirmed to contain only *Bacterium lactis*, and those that had remained sweet contained no visible bacteria. Lister therefore confidently announced that lactic acid fermentation was caused by the *Bacterium lactis* he had isolated. Lister’s proof was in these experiments, and in logical inferences from them. Having brought all the glasses safely from Edinburgh for the lecture, Lister removed the protective lid from one of the uncurdled ones, poured some out and drank it before the audience in the Great Hall, suggesting that any interested gentleman present might try it, too.40

Disposing of the argument that someone might yet promote—that *Bacterium lactis* was coincidental not causal, an accidental concomitant of the real ferment—Lister answered that it was ‘inconceivable that these two accidentally associated things should be present in exactly the same numbers’, that ‘wherever there was a fermentation particle there was a bacterium, and wherever there was a bacterium there was a fermentation particle.’ This, he said, was doubly inconceivable, and, indicating the genuine absurdity of an idea that had diverted investigators for far too long, he announced: ‘I say it would be again inconceivable that they should accompany each other in pairs.’ Each inconceivability would have been sufficient, he said, to show that the fermentation of milk required no further explanation than the action of the bacterium.

*Bacterium lactis*, Lister further concluded, had no spores. This was a point of considerable importance, because bacteria so far studied by others—including *B. subtilis* and *Bacillus anthracis*—had been shown—like fungi—to have a spore state. Lister’s supporting evidence for this important conclusion was essentially statistical. Had ‘spores or germs’ been present, the effect would have been proportionately greater than it was in the event, and his careful titrations would not have worked as they evidently had: ‘we should have the effect more than in proportion to those bacteria we have.’ *Bacterium lactis*, Lister asserted, was capable of multiplying *without* spores. It was itself the germinal particle: it constituted in itself a ‘generative apparatus’.

Lister wound up his lecture by urging the audience to ponder seriously all he had said, hoping they would agree with him that there was now ‘absolute evidence’ that *Bacterium lactis* was the cause of lactic fermentation in milk. He saw his work, he said, as a sure step ‘in the way of removing this important but most difficult question from the region of vague speculation and loose statement into the domain of precise and definite knowledge.’

**Conclusions**

In his published work Lister tended to emphasize the clinical success of antisepsis rather than the results of his own pioneering private microbiological researches. History has largely followed suit. For much of his working life, theorizing about the ‘germs’ of microbial life was controversial: long-standing arguments concerning the causes of
disease had made the topic a hornets’ nest. Soon after Lister had stirred up controversy by mentioning germ theory in his 1867 *Lancet* articles on antisepsis, a letter of sensible advice from his father laid out the strategy that Lister subsequently adopted:

> what seems to me important is . . . not to defend the Germ Theory, which might be left to take care of itself, but to describe distinctly the Treatment adopted by thee (with the theory suggested) and to show by Cases the remarkable results of thy treatment with its progressive improvements, in contrast to those results which follow the usual course of practice.41

For much of his career, the study of microbiology was a sustained counterpoint to Lister’s professional clinical work: an aspect of his life and achievement that deserves greater attention than hitherto it has received. Seen in the context of its time, this 1877 lecture at King’s College can be appreciated as highly significant, both nationally and internationally: a practical demonstration of scientific and surgical complementarity.42 Lister presented by public demonstration the first pure bacterial culture in the history of science, and the novel method—now known as serial or limiting dilution—by which it had been obtained.43 The manner in which he had developed this series of experiments, it has been suggested, could be considered ‘the prototype of Koch’s Postulates’.44 Using *Bacterium lactis* as a model, Lister indicated the direction of study required to understand and tackle the analogous organisms he believed to be responsible for hitherto ubiquitous and murderous sepsis—in wounds, punctures, incisions and fevers.45 When one considers the significance of his experimental results, Lister’s rhetoric was surprisingly spare.

Lister’s language and props suggest that he was keenly aware how unfamiliar the bacterial world would be to most of those present; to be understood, this unseen domain must be explained simply, its effects materially demonstrated. In this way, Lister encouraged his audience to recognize the insufficiency of traditional chemistry to explain the complexity of the unfamiliar world of microscopic organisms. Lister provided enlarged images of yeast and bacteria to overcome the difficulties of scale involved in the study, and the variety and ubiquity of microorganisms, and their need for appropriate conditions for growth, were demonstrated by means of diagrammatic morphology, colour and scale, and by the behaviour of the contents of his flasks, liqueur glasses and test-tube clusters.

The wide reach of this new field of study and its accessibility to scientific investigation Lister indicated by his steady pushing of the parameters of the unknown so as finally to be able to isolate a single specific organism. He made clear that these were yet early days in the study of bacteria. Research was laborious and prone to imperfection, primarily by investigator error, a problem he made explicit more than once during discussion of the appearance of unexpected organisms in his own samples: ‘was it that I had not been sufficiently careful?’ His audience was thus helped to understand the process of contamination, the ubiquity of its agents and the need for extreme care—including sterilization, specialized equipment and the refinement of procedure—to prevent it. The need for a new precision in biological scrutiny was well conveyed.

Along with the narrative and practical demonstration of his scientific findings, Lister provided tools for thought, so that his audience might think matters through, and address and comprehend their own experience. In mentioning the cow house, the dairy and the orchard, the prevailing weather conditions, and their differing impacts on the various organisms collected in his apparatus, Lister was raising not only the variety and ubiquity of these agents, but the variability and locality of their action. Hitherto the presence or absence of erysipelas or hospital gangrene in surgical wards had seemed occult, but by
visualizing the ubiquity in air of a wide variety of natural biological agents Lister made it easier for his audience to grasp why surgical or maternity wards were more likely than private houses to spawn and spread mortal infections. In demonstrating the infinitesimal amount of material necessary to putrefy a vessel of blood or to cause milk to sour, Lister allowed his audience to comprehend how even the smallest accidental or surgical exposure—merely a needlestick—was sufficient to engender bacterial spread. In diluting his bacterial mix by a million parts and showing the statistical reality of its multiplying effect in milk, he gave his audience the means to understand events by mathematical probability, and simultaneously rendered redundant the concepts of ‘concomitants’ and ‘spontaneous’ generation. Once amenable to this kind of study, bacterial life no longer need be inexplicable or mysterious.

Along with its science, Lister’s lecture is infused with metaphorical thinking, all the more effective because he did not emphasize it. When he spoke of the minute amount of bacterial matter required to spread through the mass of his pure samples and putrefy the ox blood or sour the milk, he was speaking metaphorically about the way in which a human body could be irrevocably invaded by sepsis or other infections. By twice mentioning needles, Lister indicated the danger posed by surgical instruments and the hands that hold them. The skin of the grape stood metaphorically for the human skin; the passive contents of Lister’s open test tubes for surgical or accidental wounds; the ox blood for human blood; the mass of the milk for human tissue; the cowshed and the dairy for hospital wards; the pigments in his posters for the multifarious array of infective agents; the Bacterium lactis for organisms as yet unnamed, conveying death.46

Milk—which has been souring ever since humans domesticated the cow—had not been analysed in this manner before. The fact that Lister did it so deftly deserves celebration at this centenary. Lister is not generally known for having demonstrated the first pure bacterial culture, nor for the brilliantly simple technique he devised to titrate down to single bacteria and double-test the resulting culture: nor for anticipating the postulates before Koch had formulated them.47 Lister’s work provided a unified explanation for sepsis and contagion, by demonstrating that a microorganism could be carried by air, liquid and injection, and—crucially—that it was self-propagating: its self-reproduction by division, and exponential growth in the appropriate medium, did not necessarily require the notion of a separate germ or seed.

In this landmark lecture at King’s College, Lister presented the post-hoc justification for his life’s work on antisepsis. In displaying his experiments, Lister demonstrated to colleagues, to contemporaries and to a cohort of new students that barely visible microscopic entities might live, multiply and effect the transformative process of fermentation, and by implication, of inflammation, suppuration and putrefaction, what we term infection. Lister had defined and proved by experiment the vanishingly small quantity of material necessary to instigate the process. The simple manner in which he addressed the activity of microscopic organisms in three fundamental fluids—wine, blood and milk—and the import of his findings, renders Lister’s lecture a foundational text of microbiology.

ACKNOWLEDGEMENTS

I thank Gerhard Drews and Melvin Santer for kind assistance at the outset of this work. ‘Epicanis’ of the Big Room website helped, too. Dr Sam Alberti, Louise King and other
staff at the Royal College of Surgeons of England have been hospitable and generous in allowing me access to the Lister materials in the College Collections. I should also like to thank Professor Michael Slater; friends at the Quekett Microscopical Club at the Natural History Museum, London, especially Dennis Fullwood; and staff at the British Library, the British Museum Prints and Drawings Department, at the Wellcome Library, at King’s College Archives and Special Collections, and at the Natural History Museum. Brian Hurwitz read and commented helpfully on successive drafts. I also thank my peer reviewers. This paper is dedicated to the memory of Professor Howard Gest.

NOTES

1 Lister’s Pathological Society lecture, ‘On the Lactic Fermentation and its bearing on Pathology’, was delivered on 18 December 1877, and published in Trans. Pathol. Soc. Lond. 29, 425–467 (1878) [referred to here as Lister’s Pathological Society paper]. This version of Lister’s work on Bacterium lactis is now most generally cited, possibly because Lister was much more explicit about its implications for the study of human disease and about his investigative methods. It presents closely similar materials to those in Lister’s earlier 1877 address (see notes 2 to 4 below), adjusted for a pathology-literate audience, and with emphasis on the technicalities/implications. The vote of thanks was made by Charlton Bastian, the great opponent of the idea of germs, airborne or otherwise. Lister made no recorded reply. The Pathological Society paper has since been reprinted in T. D. Brock, Milestones in microbiology (ASM Press, Washington DC, 1998), pp. 58–64, and discussed in W. Bulloch, History of bacteriology (Dover, New York, 1979), pp. 222–223. It also has a prominent place on the internet: ‘Epicanis’ discusses it on the Big Room website: Epicanis (pseud.), ‘On the lactic fermentation and its bearings on pathology’, 14 November 2008 (http://www.bigroom.org/wordpress/?p=244; accessed 12 November 2012). The American Society for Microbiology features the entire text on its website (see http://www.microbeworld.org/history-of-microbiology/1870s1880s/297-1878-joseph-lister). Most recently Melvin Santer has recognized the importance of Lister’s findings, especially the isolation of a pure bacterial culture, his unique dilution method, the proof of bacterial specificity, and the use of Bacterium lactis as a model organism. See M. Santer, ‘Joseph Lister: first use of a bacterium as a “model organism” to illustrate the cause of infectious disease of humans’, Notes Rec. R. Soc. 64, 59–65 (2010). My work supports Santer’s conclusions while addressing an earlier presentation of Lister’s work. These distinctions are important for the mid 1870s: Bulloch (see above) and Weiss, for example, date Lister’s dilution method to the publication of the Pathological Society paper in 1878. See R. A. Weiss, ‘Robert Koch, the Grandfather of cloning?’ Cell 123, 539–542 (2005).


The manuscript transcript version of the lecture which survives among Lister’s papers is entitled ‘Address at the opening of the Medical Session of 1877’ and is referred to hereafter as ‘1877 Transcript’; Archives of the Royal College of Surgeons, London MS0021/4/2 ['Folder 53’]. Lister usually lectured extempore without notes, sometimes employing a shorthand writer to record what he had said for his own record: R. J. Godlee, *Lord Lister* (Clarendon Press, Oxford, 1924), p. 314. This transcript appears to be the source for both published versions of the lecture, but seems to have been commissioned by the *British Medical Journal* and given to Lister later. Linguistic analysts have independently observed that Lister exhibits signs of oral transcription in his published writings; see J. J. Connor and J. T. H. Connor, ‘Being Lister: ethos and Victorian medical discourse’, *Med. Humanities* 34, 3–10 (2008).

Lister, ‘*BMJ* 1877’.


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Diseases such as glanders, silkworm disease, anthrax, mycetoma, relapsing fever, typhoid and leprosy had all been associated correctly with ‘low’ forms of life before 1875. Others, such as cholera, were under very strong suspicion. The late 1870s to 1880s saw an explosion of confirmatory findings to a convincing standard of proof, and the important addition of tuberculosis and malaria. For the position in Germany see C. Gradmann, ‘Isolation, contamination and pure culture’, *Perspect. Sci.* 9 (2), 142–172 (2001). For the danger of ‘instrumental infection’ (i.e. transmission) see J. Lister, ‘On recent improvements in the details of antiseptic surgery’, *Lancet* i, 401–402 (1875).


J. Tyndall, ‘Researches on the Deportment & Vital Resistance of Putrefactive and Infective Organisms, from a Physical Point of View’, *Proc. R. Instn* 8, 467–477 (1875–78). Tyndall presented this work conclusively to the Royal Society in 1877: J. Tyndall, ‘Further Researches on the Deportment & Vital Resistance of Putrefactive and Infective Organisms, from a Physical Point of View’, *Phil. Trans. R. Soc. Lond.* 167, 149–206 (1877). ‘Putrefactive’ and ‘infective’ here indicate nuances of meaning at the time; J. Tyndall, ‘Fermentation, and its bearings on the phenomena of disease’, *Fortnightly Rev.* NS 20, 547–572 (1876). There was still no adequate explanatory mechanism as to why antisepsis worked, yet Lister’s rapturous reception in Germany in the summer of 1876 shows that its adoption had brought a remarkable change in surgical survival rates. The remedy predated an explanation. Up to that date both Lister and Koch had been working in their own domestic laboratories. Koch was starting his career in bacteriology as Lister was leaving it: 1876–77 was the key year of overlap. Tyndall had heard about Koch’s first research on splenic fever from Ferdinand Cohn, who was visiting London that autumn.

Bell, *op. cit.* (note 14).

F. J. Bell, ‘Further Researches into the History of the Bacteria’, *Q. J. Microsc. Sci.* 17, 81–92 (1877). The paper, published in Cohn’s journal in Breslau, did not feature several innovations for which Koch is now renowned—plate propagation, gelatine/agar cultivation, or his postulates—all of which were developed at later stages in his career. In 1876–77 Koch was using animal blood or serum, and aqueous or vitreous humour as growth media. See Gradmann, *op. cit.* (note 9).


Lister had also used Pasteur’s solution, turnip infusions, and urine: J. Lister, Commonplace Books MS0021/4/9 (4 volumes: 1870–1873, 1873–1879, 1878–1885, 1886–1899), Archives, Royal College of Surgeons, London. See also Lister, *op. cit.* (note 1) and *Lancet* ii, 918–921 (1877).

Lister’s surviving Commonplace Books date from 1870, when he was already working on ferments (see note 21). He had been working on blood coagulation in Edinburgh as early as 1858; see, for example, his manuscript ‘At the City Slaughterhouses Edinburgh, 27th Feb
1858’, and other items in RCS MS0021/4, Archives, Royal College of Surgeons, London. It is not known whether Lister had attended the lecture in Edinburgh in November 1855 at which Thomas Southwood Smith spoke of the transmission of animalcules in contaminated air and wounds and their effects as ferments, or indeed whether Pasteur knew of it; T. S. Smith, *Epidemics* (Edmonston, Edinburgh, 1856).

Lister’s Pathological Society paper included his own admission of a serious error in suggesting pleomorphism in an earlier paper caused by contamination of his samples: ‘next to the promulgation of new truth, the best thing, I conceive, that a man can do, is the recantation of published error’; Lister, *op. cit.* (note 1).

J. Lister, Commonplace Books (see note 22).


Made with a camera lucida, a prism lens fitted to the top of the microscope. When the objects under his gaze were moving, Lister used a micrometer to measure their relative sizes and relations; Lister, ‘*BMJ 1877*’, p. 468.


For the history of the Bunsen burner see M. Barnet, ‘The social relations of the Bunsen burner’, *Chem Rev.* 2 (3), 26–29 (1993). The Petri dish belongs to the mid 1880s; see Brock, *op. cit.* (note 1), at p. xii. For Lister’s use of ‘heated’ in his 1877 Address see Lister, ‘*BMJ 1877*’. For ‘roasted’ see, for example, Lister’s Commonplace Books, vol. 3, p. 415 (1877) (note 22). For his apparatus see the Pathological Society’s report of his paper, *op. cit.* (note 1), and Lister’s Commonplace Books (note 21). The micropipette Lister designed and had made for these experiments is shown in figure 5.

The idea had been Liebig’s and had recently received fresh support from Theodore Billroth; see Santer, *op. cit.* (note 1). In the UK its main proponent was Charlton Bastian; see J. K. Crellin, ‘Airborne particles and the germ theory’, *Ann. Sci.* 22, 49–60 (1966). Burdon Sanderson vacillated. See also Worboys, *op. cit.* (note 2), p. 87.

The restraint was consciously necessary. Lister was evidently irked by those who continued to hold such views, and is recorded later in the lecture as having said: ‘It is very difficult sometimes to avoid an offensive expression.’ Lister, ‘*BMJ 1877*’, p. 467. He was aware that lives were being lost while these arguments were being batted to and fro. Lister had already expressed his own readiness to blush for the unscientific character of his own profession, and the deficient scientific education—in both chemical physics and logic—of those whose loose commentary was sometimes heard on this matter: J. Lister, ‘Address in Surgery’, *Br. Med. J.* ii, 225–233 (1871).

The shorthand writer did not record whether Lister himself sniffed the air under the glass cap, which from his words sounds likely. Odour is one of the most noticeable points of record in Lister’s Commonplace Books—he regularly noted and described the subtleties of the odours produced in his experiments, and I think for him it was highly important to raise this point before a medical audience in London, where the reek of infected surgical wards was a daily experience. Lister’s wards in Edinburgh had been sweet for years. ‘Mawkish’ is Watson Cheyne’s word for the smell: Cheyne, *op. cit.* (note 6), p. 4. See also J. Lister, ‘Address in Surgery’, *Br. Med. J.* ii, 225–233 (1871).

The state of the wards at King’s College Hospital had been a real shock for Lister and his team when they first arrived, the more so because they knew that the stench presaged deaths. Godlee noted, ‘in these wards the air was heavy with the odour of suppuration, the shining eyes and flushed cheek spoke eloquently of surgical fever’; see Godlee, *op. cit.* (note 4), p. 417.

In the 1877 address Lister referred to this image as a ‘rough diagram’: Lister, ‘*BMJ 1877*’. The poster still exists in the Archives of the Royal College of Surgeons, London, shelfmark MS0021/6/1/31. It was painted by Lister’s wife, Agnes, and/or his nephew Rickman Godlee. See Godlee, *op. cit.* (note 4), p. 275. The greyness may suggest that Lister worked without stains.

Godlee, *op. cit.* (note 4), pp. 266–267. Milk was also a highly important topic in epidemiological circles, where in the mid 1870s it was highly newsworthy; see the splendid paper by J. Steere-Williams, ‘The perfect food and the filth disease’, *J. Hist. Med. Allied Sci.*
65. 514–545 (2010). Koch used convenience for justification in using mice in his anthrax experiments; see Bell, op. cit. (note 18).

35 Cohn had also studied the formation of cheese; see Bell, op. cit. (note 14).

36 Lister had presented an earlier stage of this research in 1873, when he gave the bacillus the name Bacterium lactis. See J. Lister, ‘A further contribution to the natural history of bacteria and the germ theory of fermentative changes’, Q. J. Microsc. Sci. 13, 381–408 (1873). The lower case ‘b’ for Bacterium lactis, throughout the coverage of Lister’s 1877 address in ‘BMJ 1877’ suggests that the transcriber, editors, printer and proof-readers of the British Medical Journal were unaware of the convention, and that Lister did not have an opportunity to correct the typeset version before it was printed in the British Medical Journal. The organism is now known as Lactococcus lactis. See M. Teuber, ‘The genus Lactococcus’, in The lactic acid bacteria (ed. B. J. P. Wood & W. H. Holzapfel), vol. 2, pp. 173–232 (Blackie/Chapman & Hall, London, 1995).


38 The poster was painted by Lister’s nephew Rickman Godlee. See Godlee, op. cit. (note 4), p. 275. It, like the one of yeast and Bacterium lactis already mentioned, survives in the Archives at the Royal College of Surgeons, London: MS0021/6/1/22. It was reused at the Pathological Society meeting, and a printed version appeared in that society’s Transactions and in Lister’s Collected papers.

39 In the Commonplace Books, op. cit. (note 21), the cow is actually named as ‘Blackie’. Figure 3 shows Lister referring to this particular cow in the text surrounding the image of his test tubes. Commonplace Book 3, p. 240 (1877).


41 J. J. Lister, letter to Joseph Lister (20 March 1868), Wellcome Library Archives, WMS6965/59.


45 Santer, op. cit. (note 2). Ashley Miles observed that ‘urine, milk and egg-white served as experimental models for the healthy wound’: Miles, op. cit. (note 2).

46 The lecture carries a penumbra of theological implication, involving blood and wine, the sacrament, purity and contamination, life, nurture and death. The validity of addressing Lister’s metaphorical and spiritual turn of thought is confirmed when we see that Lister had told his Edinburgh students at their graduation in 1876: ‘it is our proud office to tend the fleshly tabernacle of the immortal spirit’; quoted in Godlee, op. cit. (note 4), p. 391.

47 Epicanis (pseud.), op. cit. (note 1). Harvey Cushing later wrote: ‘Pasteur had written to Bastian in July 1877: “Do you know why I desire so much to fight and conquer you? It is because you are one of the principal adepts of a medical doctrine which I believe to be fatal to progress in the art of healing—the doctrine of the spontaneity of all diseases.” The younger generation sat back and watched the tilting of these giants, and, until Tyndall entered the lists on Pasteur’s side and finally Lister, English-trained youths were naturally imbued with the ideas of spontaneous generation’; see H. Cushing, The life of Sir William Osler (Oxford University Press, 1940), vol. 1, p. 164. Evidently, to Osler’s generation of young men, Lister’s microbiological demonstration was regarded as conclusive.