Forgotten microbiology – back to the future

Milton Wainwright

Microbiologists striving to solve problems in the 21st century could well find some answers in the publications of their predecessors…

University libraries all over the world are full of old scientific journals and books, left unread to gather dust. They are ignored largely because most scientists, including microbiologists, think that anything that is more than, say, 10 years old is not worth bothering with. Here, however, I want to suggest that these journals represent a huge resource of untapped knowledge, a view substantiated by numerous examples of where discoveries turn out to be independent re-discoveries. For example bacteria, including spiral forms, have long been isolated from stomach ulcers and antibacterial bismuth compounds have similarly long been shown to be effective in treating gastric ulcers. Imagine the suffering that could have been saved had these observations been acted upon before the mid-1980s when *Helicobacter pylori*'s causal rôle was discovered. Incidentally, bismuth was also used to treat rheumatoid arthritis and lupus erythematosus; could these diseases also be bacterial in origin?

The reasons why the older literature has often been ignored are varied and complex. One-off reports, for example, may just have been overlooked, or discoveries may have been dismissed because of opposition from a single, influential person. The minor unwritten law of science that '*one negative result (or a few) often outweighs many positives*' often operates, as it did in the case of mitogenetic radiation (an idea supported by a vast, international literature) that was effectively dismissed by a single negative report. The '*but everyone knows it is wrong*' response is often seen to be particularly damaging to new ideas, especially as it is often used by people who are ignorant of the relevant literature!

Of all the forgotten papers, those relating to the aetiology of disease are likely to be the most important. Some of the historical claims that bacteria cause diseases generally thought to be non-infectious, including cancer, rheumatoid arthritis and multiple sclerosis, are currently being re-evaluated, often with exciting results. What a tragedy it would be if the recent findings of Ebringer and co-workers, that rheumatoid arthritis and BSE have a bacterial aetiology, were, like much of the older literature, to be neglected for the best part of a century.

Filterable bacteria and extreme bacterial pleomorphism

Many microbiologists working during the early part of the twentieth century claimed that bacteria could pass through filters and then grow on standard media. These so-called filterable viruses were said to cause diseases, including rheumatism, arthritis, meningitis, influenza, the common cold and even cancer. When viruses (in the modern sense) were discovered the research effort shifted towards these agents and the exciting work on filterable bacteria slowly disappeared, only to reappear more recently in the modern guise of so-called nanobacteria. As early as 1917, the American scientist George Foster isolated a 'filterable virus' which, he claimed, caused colds; this turned out not to be a virus, but a filterable bacterium. Similarly, Olitsky & Gates isolated a filterable bacterium (0.15–0.3 μm, the so-called *Bacterium pneumosintes*) which, they claimed, caused a mild influenza-like infection pre-disposing the patient to pneumonia. During the 1920s and 1930s, it was also suggested that the massive death toll from the 1918 'flu pandemic resulted from synergism between viruses and bacteria (including filterable types).

Reports that cocci can change into rods and filaments and back again are a common feature of the early bacteriological literature and some workers even concluded that bacteria undergo life cycles, often with a hidden or filterable stage; a view given its modern expression in the fascinating book, *Cell Wall Deficient Forms* by Lida Mattman. As she points out, the rôle of bacterial L-forms in diseases such as cancer and arthritis is well worth a second look.

The cancer germ

For over a century, it has been claimed that highly pleomorphic, intermittently acid-fast bacteria cause cancer. It is a major disgrace that this literature has been ignored, especially since evidence was produced to show that tumour-isolated bacteria could be used to produce effective anti-cancer vaccines, and also cause tumours when injected into experimental animals. The historical finding that stomach cancer is associated with highly organic soils, together with the recent finding that *Helicobacter pylori* possesses amidases, typically found in soil bacteria, also suggests the possibility that 'cancer soils' may contain large numbers of this bacterium.

The sheer variety of non-virus isolates associated with cancer over the last century suggests that onco-genesis may well be a common ability amongst viruses and non-virus micro-organisms, working in concert with environmental and cellular factors, and genetic pre-determinants.

Forgotten antimicrobial agents

The increase in antibiotic resistance amongst pathogenic bacteria has led many to speculate (perhaps prematurely) that we are approaching the end of the antibiotic era. Gene therapy is probably the favourite choice to replace antibiotics but, if desperate, we might also reconsider some historical approaches. For example, in the past, diseases were controlled by a variety of biocontrol agents, including bacteriophages, moulds and bacteria. Maggot therapy, the use of living fly larvae to treat infections, has recently made a spectacular comeback. Bacteria and viruses were also used to treat cancers and bacterial infections, so-called 'fever therapy' (where infections are given to induce a high fever).

Forgotten chemical approaches to disease control include the use of pectin and urea; urea, by the way, is naturally produced by fly larvae during maggot therapy. Extracts of organs (organ therapy) or bodily fluids, like bile, were also used against bacterial infections, while lysozyme was used to treat infections in Russia during the late 1930s.

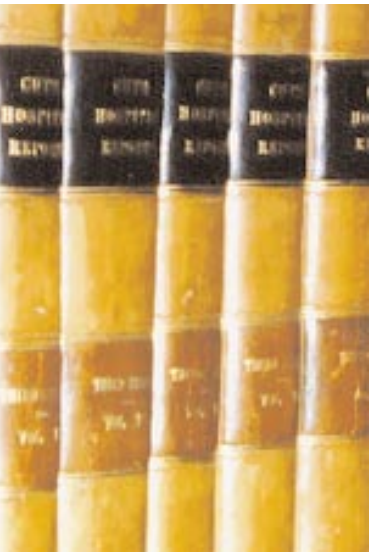
Unpurified penicillin filtrates were also shown to have anti-tubercular, antidotal and even anti-tumour properties; by purifying penicillin we may therefore have thrown out a few babies with the bath water!

Action at a distance

The older literature suggests that micro-organisms can communicate using non-chemical signalling (i.e. action at a distance), the best example being by producing growth-stimulating, low intensity UV light (i.e. mitogenetic radiation). Micro-organisms have also been shown to grow towards metals, not ions, but lumps of metal, including iron and copper. Perhaps the best illustration of action at a distance is seen in the fungus *Phycomyes nitens*, which is attracted to iron, a phenomenon historically attributed (by Errera) to its ability to detect, and grow towards, water contained in the iron.

Panspermia and the origin of life

The eminent Victorian physicist, Lord Kelvin is usually credited with the view that life on Earth originated from space. More recently, the idea has been extended and popularized by Sir Fred Hoyle and Chandra Wickramasinghe. After years of being ridiculed, the views of these two scientists are now being taken more seriously; note, however, how their names are mysteriously omitted from recent articles on the subject! The soil microbiologist Jacob Lipman suffered much similar ridicule when he claimed that he had found bacteria in meteorites, a possibility which today is taken very seriously. Even the view, generally ascribed to Lynne Margulis, that cellular organelles are symbiotic accumulations of previously free-living organisms was once referred to as that '*old chestnut*'. Yet another recently resurrected, but old idea is so-called chemical photosynthesis (first described towards the end of the nineteenth century by Benjamin Moore), namely that ferric oxide and carbon dioxide, in the presence of light, yield formaldehyde, a precursor of life.



Conclusions

As I hope I have shown, there exists much forgotten, and often untested, literature relating to micro-organisms. How much of this is correct is obviously open to debate. Most microbiologists would, I assume, readily dismiss much of what I have discussed, perhaps with good reason, but I am sure that there is much of value here. Perhaps research councils and medical charities might even consider funding searches of the older medical microbiological journals to seek out forgotten research. The information could then be considered by what might be called 'hindsight committees'. I guarantee that these would prove far more productive than so-called 'foresight committees'.

Finally, if you think that microbiology cannot get much stranger, try reading the historical, and more recent, literature on paranormal microbiology which suggests that the human mind can influence the growth of micro-organisms.

Although limitations of space have allowed me to merely touch upon the forgotten literature, if only a small portion of what I have discussed is true then we are in for an exciting new millennium.

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Further reading

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