

It's time for a change of paradigms!

Why microbiology needs to reconsider

by Dr. Jiri Snaidr

Newborn babies are often infected and die by bacterial infections. Rare tragedies? The current case of bacterial infections at the University Medical Centre of Mainz caused by contaminated infusions shows tragically how far humans are behind fighting bacteria.

During the last 15 years new bacteria detection methods showed that microbiologists are in fact only aware of what is a very small part of the actually existing bacteria. The large majority of microorganisms stays hidden. The reason for this is that conventionally used cultivation procedures are only able to detect more than 1% of all bacteria contained in environmental samples.

Furthermore, studies indicate that microbial diversity is far more extensive than recognised before. Despite the fact that the majority of bacteria species is not yet identified and that the years ago set number of them had to be corrected drastically, microorganisms are routinely still detected by the application of the "gold standard" procedure using artificial cultivation media. This "gold standard" method, which had been invented when experts were still unaware of the actual extend of bacterial diversity, proves to be painfully slow compared to newly available methods.

The outdated "gold standard"

Cultivation of bacteria on artificial nutrient media has been the "gold standard" in bacteria detection for more than 100 years. Despite its well known restrictions this method still forms the basis of most established detection procedures. A thought experiment: If today's detection technologies were to be the long established "gold standard" and cultivation were to compete – it wouldn't have the slightest chance. Why not? First of all, cultivation is based upon the idea that bacteria grow on artificial nutrient media which in fact only works in the minority of cases. Second, cultivation generally supports the phenomenon of "population shifts".

Bacteria groups matching the medium will grow faster than the ones not matching. The latter will thereby be "overgrown" by fast growing other groups and thus will potentially not be detected. Even if the bacteria grew on the medium it would still take an additional procedure in order to specifically identify the bacterium. This cultivation method is therefore imprecise and insufficient as well as too

slow to provide real microbiological safety.

Focussing on pathogens/indicator organisms often limits safety

However, not only the method but also the systematics of microbial analysis has to be changed. Due to the generally applied cultivation method's limitations a particular sample is only analysed for particular bacteria. Thereby, the sample is either tested for pathogens or for indicator organisms. The latter, if tested positively, indicates the occurrence of considerably more dangerous bacteria. In case general analysis is conducted (total bacteria amount) this method is also based upon cultivation on nutrient media. Negative results thus merely indicate that bacteria did not grow on a particular medium. Whether other non-cultivable bacteria are contained in the sample cannot be concluded. Therefore, safe sterility cannot be guaranteed. In standard microbiology, unfortunately, over the decades, a certain routine was established which prevented most analysts from questioning the "gold standard" or the approach of analysing pathogens/indicator organisms. Seen from this angle it surprises that in certain sensitive areas it isn't a permanent goal to first detect all viable bacteria by a safe method – even without knowing their name – in order to analyse them more specifically afterwards.

The FISH method

The Pharmacopoea Europaea recognises a therein established alternative method which allows rapid analysis without cultivation: the FISH method. The Pharmacopoea Europaea comprises recognised pharmaceutical standards concerning quality, monitoring, storage and designation of pharmaceuticals as well as substances, materials and methods used in their production and analysis. The fluorescence-in-situ-hybridisation (abbreviation FISH) is a recognised detection method for both known and unknown microorganisms. It is based on the fact that, in 3.5 billion years of microbial evolution, every bacterium has developed special signatures in its nucleic acid which are specifically linked to a certain species, subspecies or whole bacteria group. For these special signatures specific gene probes can be developed. Gene probes are tiny pieces of DNA labelled with a fluorescent dye which are sent into the bacteria of a given sample. When the gene probes find their matching signatures they bind to them which keeps the dye within the cells: the bacterium begins to shine.

By applying the gene probe technology unknown as well as known bacteria can be detected unequivocally and highly specifically. The procedure does neither require cultivation nor isolation of cell components. To the contrary: by specifically visualising the complete, intact cell microorganisms can be detected specifically and directly at their site of action. Such detection procedures take less than 3 hours. In contrast, conventional cultivation procedures take 48 hours at minimum until results are provided.

Further newly invented methods in microbiology such as adenosine triphosphate (ATP) analysis, immunological procedures or polymerase chain reaction (PCR) also attempt to rid conventional cultivation methods of their shortcomings. However, they all bring along their own weaknesses which falsify the analysis results. For instance, when applying PCR it is mostly impossible to determine whether the result is based on living or dead cells or even influenced by free nucleic acid. PCR requires isolation of the nucleic acid prior to analysis which can be problematic especially in frequently conducted analysis.

VIT – an industrialised and standardised version of FISH

vermicon AG had already recognised the great potential in the FISH technology more than 10 years ago and is recognised as a specialist of its application in industry world wide. Since the company's foundation in 1997 the FISH technology has been consequently developed further and is now marketed under the company's owned brand VIT (vermicon identification technology). VIT is an industrialised and standardised version of FISH. vermicon AG teamed up many recognised experts in the field of FISH technology and holds various patents for its innovative method. During the last decade the company was able to show that applying FISH technology took the microbiological detection technology to the next level.

As long as there is no real change in microbiology paradigms further cases of illness and death as preceded by the University Medical Centre of Mainz incident will occur. Only when the authorities and industrialists in charge set the course towards profound changes in microbiology new methods such as the FISH technology have a chance of becoming microbiological routine in the industry. This will not only change but improve microbial diagnostics by making it sustainably safer.

The author of this article is founder and CEO of vermicon AG in Munich. ermicon AG is the specialist for detection of microorganisms. The company provides innovative solutions for any kind of microbiological problems in all industrial processes. By offering a wide range of conventional methods as well as patented technologies vermicon is always prepared to fully comply with the clients's particular needs. Additional to the wide range of services and the broad consulting portfolio vermicon also offers test kits for microorganisms: Since 2001, the patented VIT® gene probe technology is also available as convenient standardised and industrialised VIT rapid detection kits.

contact information:

vermicon AG

Emmy-Noether-Str. 2
D-80992 Munich

info@vermicon.com
www.vermicon.com