New approach of resistant tuberculosis

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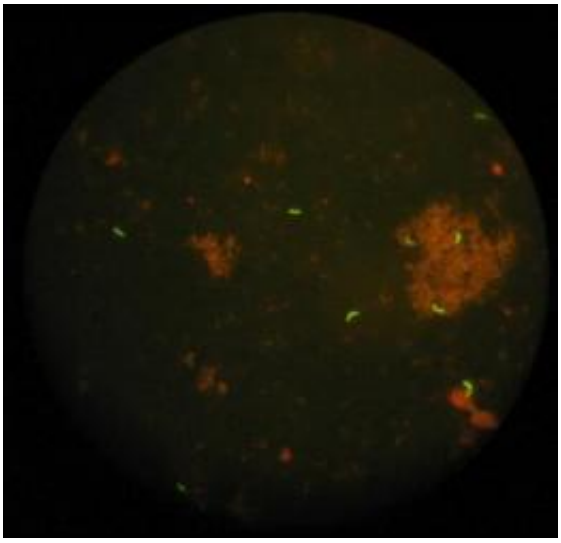

The fluorescent lines are living tuberculosis bacilli, on a background of cellular debris from human sputum. Scientists of the Antwerp Institute of Tropical Medicine gave a new application to a forgotten technique: Fluorescein diacetate staining, which only stains living tuberculosis bacilli (and not dead ones). This way they can see immediately after treatment if resistant bacilli survived. This simple technique can replace classical microscopy, now the standard procedure in developing countries, which cannot make this distinction. (Multi)resistant tuberculosis is becoming a threat to world health. © Institute of Tropical Medicine Antwerp

Scientists of the Antwerp Institute of Tropical Medicine have breathed new life into a forgotten technique and so succeeded in detecting resistant tuberculosis in circumstances where so far this was hardly feasible. Tuberculosis bacilli that have become resistant against our

major antibiotics are a serious threat to world health.

If we do not take efficient and fast action, 'multiresistant tuberculosis' may become a worldwide epidemic, wiping out all medical achievements of the last decades.

A century ago tuberculosis was a lugubrious word, more terrifying than 'cancer' is today. And rightly so. Over the nineteenth and twentieth century it took a billion lives – more than the world population in 1800. Only in the nineteen fifties it became possible to push the disease back, with newly developed antibiotics. Countless sanatoria in Switzerland were closed one after the other and converted into hotels. Today almost nobody in the industrialized world still grasps the gruesome nature of 'consumption disease'. The treatment was so successful that the World Health Organization (WHO) in 1960 decided to eradicate tuberculosis once and for all. It almost worked.

But Mycobacterium tuberculosis is a tough adversary, demanding a treatment with several antibiotics simultaneously during months on end. Hardly feasible in developing countries. The numerous erratic or halted treatments led to growing numbers of bacilli that were resistant to several antibiotics. In the early eighties the death toll first stagnated and then got up again. The arrival of AIDS in the same period made things worse, because an infection with the one makes you more susceptible to the other.

Today we witness a growing number of 'multiresistant' tuberculosis, withstanding our best medicines, and only treatable with a costly and long cure of toxic drugs. Unfeasible in developing countries. According to WHO estimations, of the 5 million or so multiresistant cases of the last decade, only one percent had access to treatment. In 1991, a tuberculosis bug in New York was found to be resistant to 11 antibiotics. Cases have been reported where each and every antibiotic was useless.

So far, these 'omniresistant' bacilli each time perished with their host before they could spread. So far, that is.

In 2012 on average 1 in 30 of new TB cases worldwide was multiresistant, with peaks of 1 in 3. With patients relapsing after a first cure, on average 1 in 5 was multiresistant, with peaks up to 65%. The highest numbers were all registered in the former Soviet Union. Without active measures the numbers will only rise.

If we want to prevent an epidemic of difficult to treat tuberculosis, then resistant cases, which do not react to the normal treatment, need to be recognized as early as possible, and immediately treated with second-line antibiotics that still work. But the laboratory tests to identify resistant TB bugs are cumbersome – the WHO estimates that in 2009 only 11% of multiresistant cases were discovered.

Checking smears under the microscope still is the recommended technique for TB screening, but it cannot differentiate between living and dead bacilli. So you do not know if you are looking at the cadavers of a successful treatment, or at resistant survivors. Only if the numbers after a long wait still don't fall, you know you are dealing with a resistant strain. But all that time the patient has remained contagious.

With high-tech PCR technology one can immediately ascertain if the bacillus is from a resistant strain, but in practice and certainly in resource-limited countries this is unfeasible. It also is impossible to cultivate every sample and then bombard it with every possible antibiotic to survey which ones still work for that individual patient.

Armand Van Deun and colleagues therefore gave a new application to a forgotten technique: vital staining with fluorescein diacetate (FDA). It only stains living TB bacilli, so one immediately sees those bacilli escaping treatment. The scientists improved the detection of the

luminous bacilli by replacing the classical fluorescence microscope with its LED counterpart. Together with colleagues in Bangladesh they tested the approach in the field for four years. This was made possible by a grant from the Damien Foundation – another possible sponsor had fobbed them off because their technique was too unknown.

But their approach works, also in a poor country. If after treatment the FDA-test was negative, in 95% of cases more elaborate tests didn't find active bacilli in the patient's sputum either. And if the test was positive, you could bet your boots that you had found a resistant bacillus.

This simple test allows, also in resource-limited labs, to detect a high number of resistant TB bacilli that otherwise would have been discovered too late or not at all. The scientists report in the *International Journal of* Tuberculosis *and Lung Disease* that three times more patients could directly switch to the correct second-line treatment without losing time on a regimen ineffective against their resistant bacilli. On top of that, the technique can cut in half the number of cases where doctors start a retreatment 'just to stay on the safe side', because it ascertains that the bacilli detected by the classical microscopy in fact are dead ones, which do not require further treatment.

More information: The article “Fluorescein diacetate vital staining allows earlier diagnosis of rifampicin-resistant tuberculosis” appears in the International Journal of Tuberculosis and Lung Disease and has been released as e-pub ahead of print. www.ingentaconnect.com/content … 16/00000009/art00008

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