Silver threatens the use of antibiotics

Bacterial infections are a threat to mankind and, irrespective of geographical, cultural, gender or age factors, bacteria have always been a major cause of morbidity and mortality. The introduction of antibiotics during the Second World War, changed the picture radically and today antibiotics constitute the group of pharmaceuticals with the highest consumption worldwide. However, the use of antibiotics is not without problems. It is only relatively recently that we have started to realize how complex and serious the consequences are, not just for the individual patient but also for Health care in general.

Antibiotics are toxic to bacteria. Toxic heavy metals are also toxic to bacteria. The mechanisms bacteria use to protect themselves against these substances are, to some extent, the same: they alter their cell wall or cell membrane and expel the toxic substance via so called efflux pumps (Li 1997, Rose 1999, Melhus, manuscript). Some Gram-negative environmental bacteria, i.e. bacteria which are found practically everywhere in our environment, may also accumulate silver inside their cells. This feature in the Acinetobacter and Pseudomonas spp. has been exploited for industrial use but not for medical purposes (Shakibaie 1999). Gram-negative environmental bacteria are frequently resistant to most antibiotic groups, and they may also develop resistance relatively fast during treatment. Therefore, it is not surprising that Acinetobacter and Pseudomonas spp. ravage intensive care units globally, persistently challenging the infection control measures.

When the bacteria alter their cell walls or cell membranes to protect themselves against silver, this may render one of our most important antibiotic groups ineffective. This group is called beta-lactams. The cell walls are its modus operandi and this group represents 50% of antibiotics consumed. Efflux pumps may be aimed at pumping out one or a few substances but there are also multi-drug pumps. The latter kind is able to expel toxic heavy metals, disinfectants and antibiotics. Again, the antibiotic group which is most affected is the beta-lactams, but quinolones and aminoglycosides, agents which kill bacteria rapidly and are used chiefly on patients with defects in their immune system or with life threatening infections, are also affected.

Genes that code for efflux pumps are localized on the bacterial chromosome or in a plasmid, a small ring of genetic material. So far, silver resistance genes have only been found on a certain type of large plasmids which also carry multiple genes encoding antibiotic resistance (Gupta 2001). To carry plasmids requires extra energy. Bacteria may therefore lose plasmids unless the advantages of keeping them override the disadvantages. In an environment with a constant exposure to silver it may be advantageous to keep them. Silver can therefore constitute a part of a selective pressure and may actively contribute to the spread of antibiotic resistance. We know that this has happened, despite the fact that only a few microbiology laboratories have the capacity to investigate the matter (Rosenkranz 1974, McHugh 1975, Bridges 1979, Markowitz 1983, Mayer 1086, Pirmay 2003, Ip 2006). The most vulnerable units are the burn units in tertiary care centers where the use of both silver and antibiotics is frequent. Unfortunately, the use of silver is now increasing, not only in Health care but in homes and public places, as well. The bacteria will therefore, quite unnecessarily, be exposed to an increased selective pressure and the long-term consequences of this are hard to assess. There is no scientifically documented case where silver has saved the life of a patient with a life-threatening infection. Antibiotics, however, have done just that.
Is it then difficult to induce silver resistance in a bacterium? No, in a laboratory it can be accomplished relatively fast (Warriner 2005, Melhus, manuscript) and at the same time it is noticeable how the susceptibility to antibiotics is affected. Silver resistance is most easily developed in bacteria with already documented resistance mechanisms to antibiotics, such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), enterobacteria with production of extended spectrum beta-lactamases (ESBL), multiresistant Pseudomonas aeruginosa, i.e. bacteria which we are constantly fighting in Health care (Melhus, manuscript). At present it is uncertain how quickly or often this occurs to bacteria outside the laboratory, but most likely the silver exposure in nature, in our homes and in Health care is already sufficient to induce silver resistance (Silver 2003, 2006, Johnson 2005).

Silver resistance associated with antibiotic resistance has been observed in isolated bacteria from birds (Johnson 2005) and in salmonella spp. (Gupta 1999). (Salmonella is a bacterium which is mainly found in animals but it may also infect humans via food and cause diarrhoea and vomiting). There are silver resistant bacteria in our mouths (Davis 2005), which may possibly be related to the silver contents in amalgam fillings. Silver resistant bacteria have also been found in nature, in food, in intestinal bacteria from different geographic locations and in our hospitals (Grewal 1999, Hendry 1979).

Silver is no solution to a problem. It is a part of the problem. With the introduction of digital cameras, the consumption of silver was dramatically reduced which made a general decrease in silver exposure for individuals as well as bacteria and the environment possible. With all that in mind Samsung suddenly allows environmental bacteria, intestinal bacteria, skin bacteria, including our most common wound bacterium Staphylococcus aureus, to become permanently exposed to silver through silver washing of clothes and textiles. If bacteria are silver resistant, how can silver kill those bacteria that are the cause of bad odours and stains on the clothes?

In view of the current knowledge, there is no reason to abandon the principle of caution. Instead, by refraining from using silver products, we must ensure that coming generations will benefit from one of the greatest achievements in medicine - antibiotics - and a relatively non-toxic environment.

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