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- Health care-associated infections remain a major cause of patient morbidity all over the world.
- Environmental contamination, hand hygiene, surface disinfection belong to the most critical factors in the acquisition of nosocomial pathogens.
- Application of the disinfectants has become an essential aid in the prevention of nosocomial infections.
- Chemical substances that form the base of the disinfectants demonstrate a multi-target activity when compared with antibiotics.
- This phenomenon contributed to the weakening of the attention paid to the disinfectant resistance problem.
- Disinfectants have been extensively used not only in hospitals and health care institutions but by general population in households, schools, sports and social activities etc.
Disinfectants – mode of action

• work environmentally = totally \textbf{different} from antibiotics and many pesticides

by \textit{absorbing onto any microbial cell} –

increased absorption and the permeability of the cell membrane -

ultimate rupture + leakage of the contents of the cell
Disinfectants – result of the action

- microbes live after disinfectant use – not because of mutations, but non-selective disinfectants

- possible miss of microbes with disinfectants

NO CHANCE OF MUTATIONS!
-However, reports from clinical microbiological labs on isolation of bacterial strains with a high resistance against disinfectants standardly used in hospital environment, raised an attention of scientists and researchers to the problem of disinfectant resistance.
In the broad ecological sense, if antibacterial chemicals are acting like antibiotics (which they are), then the consequence of use should follow that for antibiotics, i.e. resistance, will eventually emerge in time.

Stuart Levy
- In spite of the warning coming from the microbiological labs as well as from negative experience with indiscriminate use of ATB, the DP have entered widely our life. They are used for numerous purposes in industry, cosmetics, pharmaceutical products, households utensils, water treatment etc., thus creating a selective pressure on DP resistance development.

- Resistance towards disinfectants is facilitated by several mechanisms operating also in antibiotics resistance.
Antiseptic **and** disinfectant tolerance in bacteria

- **intrinsic**, in particular the ability to **sporulate**

- **adaptation** of G- bacteria

- the protective effects of **BIOFILMS** - 3,000 x more resistant than plankton
The basic mechanisms operating in antibiotics and disinfectants resistance are:

a - point mutations associated with alterations of the DP target cell structures
b - inactivation of DP by enzymes produced by microorganisms
c - cell eflux pump
d - permeability modifications in outer membrane of the microorganisms.
Examples

A- Point mutations were confirmed by discovery of:

mutation in E.coli *fabI* gen coding enoyl-ACP reductase (Fab1), involved in biosynthesis of fatty acids and was linked to resistance against triclosan.
B- The number of reports inform on isolation of mutants with a high capacity to inactivate substances that form the base of DP. QAC, aldehydes, alcohols, phenols, biguanides and halogen releasing agents are target of microbial enzymatic activity.

- Enzymes such as hydrolyses, dehydrogenases, oxidases produced by microorganisms are important aid in surviving microorganisms in the presence of high DP concentrations.
C – Efflux pump is an important mechanism contributing to the microbial resistance against DP. This mechanism is common for microbial resistance against ATB and DP. Expression of marRAB and soxRS loci in *E. coli* or in *Salmonella enterica* is always associated with activation of acrAB locus, responsible for multiresistance against antibiotics.
On the other side chlorhexidin or benzalkonium chloride activate MexCD-oprJ in *P. aeruginosa*, that controls antibiotics resistance.
D - Permeability of the cell outer membrane. Any alteration in the structure of cell outer membrane may represent a new barrier for antibiotics and disinfectants. This mechanism is active with DP for which the target structures are located at the surface or deeper in the structure of the cell envelope.
There is an increasing evidence on coresistance and cross-resistance between clinically important antibiotics and disinfectants used in a hospital hygienic program.

Outbreaks of biocide resistant microorganisms in hospital and industrial environment was reported.

Association of antibiotic resistance and biocide resistance /QAC/ was confirmed in hospital strains of *Staphylococcus* species.

Nosocomial strains *Klebsiella oxytoca* revealed a higher resistance to commonly used disinfectants than standard strains. ATB resistant G – bacteria from hospital environment showed a higher resistance to chlorhexidin.
In recent years a progress has been made in understanding the resistance mechanisms both intrinsic and acquired by mutations or by acquisition of the mobile genetic elements such as plasmids or transposons.

- The scientific literature is bringing information on functioning of both types of disinfectants resistance in different types of bacteria including spores, mycobacteria and nonsporulating bacteria.
Plasmids vs resistance of G- bacteria to antiseptics and disinfectants?

- heavy-metal resistance
  - Hg, Ag

- increased MICs have been confirmed also for staphylococci
With the progress in development of the new forms and types of disinfectants a recent studies showed that resistance can be developed against DP in nanoparticle forms. Exposure of the *Mycobacterium smegmatis* to silver nanoparticles raised at least four times the resistance not only to AgNPs but also to isoniazid.
The exposure to subinhibitory concentrations of DP caused in G+ and G– bacteria selection of the cell population with a higher resistance against a particular disinfectant thus contributing in a step-wise process to the prevalence of the resistant forms in the environment.

In this data resonates the idea that incorrectly diluted disinfectants and applied in a hospital environment represent a factor promoting the resistance of pathogens against both antibiotics and DP.
Not only scientists, researchers in microbiology labs, but authorities of WHO, EU and other international bodies are raising voice for prudent and appropriate use of microbicidal chemicals in nosocomial environment in order to minimise the risk of antimicrobial resistance.
Do not underestimate the power of microorganisms.
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