IMMUNO-VIP and IMMUNO-CIP[a)] as support in fighting against Superbug Methicillin-Resistant *Staphylococcus aureus [MRSA]*

[a)] *IMMUNO-CIP and IMMUNO-VIP: Immunologically Active Proteins obtained from hens immunized with a complex of immunogen (bacterial strains with SPGA)*

Staphylococci (colloquially named 'staph') are a common type of bacteria that live on the skin and mucous membranes (eg. inside the nostrils) of humans. Of these bacteria, *Staphylococcus aureus* (*S. aureus*) is the most frequently involved in human disease. Other *Staphylococci*, including *S. epidermidis*, are considered commensal, i.e. normal inhabitants of the skin surface [1].

About 15-40 % of healthy humans are carriers of *S. aureus*, that is, they have the bacteria on their skin without active infection or disease (colonization). The carrier sites are usually the nostrils and flexures, where the bacteria may be found intermittently or every time they are looked for [1].

Despite being harmless in most individuals, *S. aureus* is capable of causing various infections of the skin and other organs. *S. aureus* infections are common in people with frequent skin injury, particularly if the skin is dry. Staphylococcal skin infections are seen most commonly in prepubertal children and certain occupational groups such as healthcare workers. They may occur for no obvious reason in otherwise healthy individuals.

Typical clinical aspects of Staphylococcal infection:

- Hair follicle infections including Staphylococcal folliculitis, boils (furuncles and carbuncles), abscess and sycosis (beard infection)
- Impetigo (school sores)
- Ecthyma (crusted ulcers)
- Cellulitis (more often due to *Streptococcus*)
- Secondary skin infection of wounds, dermatitis, scabies, diabetic ulcers etc.
- Mastitis (inflammation of the breast) and abscess of the breast; the bacteria may pass from a breast abscess into milk
- Staphylococcal hypersensitivity reactions such as folliculitis decalvans (a cause of scarring hair loss)

Antibiotic resistance in Staphylococci

Staphylococci are becoming increasingly resistant to many commonly used antibiotics including penicillin, macrolides such as erythromycin, tetracyclines and aminoglycosides.

Penicillin resistance in Staphylococcus aureus is due to the production of an enzyme called betalactamase or penicillinase. Methicillin and flucloxacillin are lactamase-resistant penicillin.

Combinations of penicillin with a beta-lactamase-inhibitor (such as amoxicillin + clavulanic acid) may be used to treat Staphylococcus aureus infections and are sometimes effective against flucloxacillin-resistant bacteria. These antibiotics have a broad range of action against several types of bacteria and are best reserved for patients with mixed bacterial infections.

Patients who are allergic to penicillin are most reliably treated with vancomycin, although for minor infections macrolides such as erythromycin may be adequate. Macrolide resistance is also high among Staphylococcus aureus but macrolides may be taken by mouth whereas vancomycin requires intravenous administration. Other options include clindamycin and rifampicin.

Unfortunately, there is now increasing methicillin resistance in Staphylococcus aureus (MRSA)

How Common is MRSA?

MRSA is methicillin-resistant Staphylococcus aureus, a type of Staphylococcus that is resistant to many antibiotics. In a healthcare setting, such as a hospital or nursing home, MRSA can cause severe problems such as bloodstream infections, pneumonia and surgical site infections. If not treated quickly, MRSA infections can cause sepsis and death. Studies show that about one in three (33%) people carry Staphylococcus in their nose, usually without any illness. Two in 100 people carry MRSA. Data are missing regarding the total number of people who get MRSA skin infections in the community [11].

Can MRSA Infections be Prevented?

Yes. Numerous studies and reports show that when healthcare providers follow guidelines, MRSA infections can largely – if not completely – be prevented. These guidelines include a range of activities that healthcare facilities can implement to reduce or eliminate MRSA infections [8-9].

Is MRSA an Antibiotic Resistance Problem?

Yes. Staphylococci have become resistant to several antibiotics, making MRSA and other types of resistant Staphylococci major antibiotic-resistance problems. In CDC's landmark report, Antibiotic Resistance Threats in the United States, 2013, CDC listed MRSA as a "serious threat." The report was accompanied by a national plan to combat antibiotic resistance [8-9].

The spread of MRSA used to be healthcare-associated. However, recently community associated MRSA (CA-MRSA) tends to replace healthcare-associated MRSA (HA-MRSA) in some regions of the world. A study in Uruguay reviewed Staphylococcus aureus isolates from a large healthcare facility in Montevideo (the country capital) and from 3 additional hospitals. An infection was defined as healthcare-onset if the culture was obtained >48 hours after hospital admission. At Montevideo, the proportion of S. aureus infections caused by CA-MRSA increased from 4% to 23% over 2 years; the proportion caused by healthcare-associated MRSA (HA-MRSA) decreased from 25% to 5%. CA-MRSA appeared to have replaced HA-MRSA strains at the main healthcare facility in the capital. CA-MRSA appears to cause healthcare-onset infections, a finding that emphasizes the need for infection control measures to prevent transmission within healthcare settings [8].

Immuno-CIP and Immuno-VIP products as support in the fight against MRSA infections.

Biological active proteins contained by Immuno-CIP and Immuno-VIP products are prepared from eggs of hens, previously immunized with a complex of antigens consisting in: bacterial, spores, viruses and fungal antigens, and most important antibiotic-resistant bacteria (superbugs), all isolated from patients in Romanian hospitals, or from foreign patients treated in Romanian hospitals.

In order to have a more comprehensive antigen structure, seven antibiotic-resistant strains were used for each bacterial species. [3-7].

The Immuno-CIP and Immuno-VIP group of biological products were prepared by immunizing chicken and further using the resulting eggs (eggs with a significant quantity of immunologically active proteins for the complex of antigens mentioned above).

The immunologically active proteins produced by ACTIVEIMMUNITY and tested in the ACTIVEIMMUNITY laboratories demonstrated a higher degree of penetration of epithelial cells of the oropharyngeal, nasal and vaginal mucosa. Thorough studies are underway.

Use of Immuno-CIP products

Biological products are produced in the form of lyophilized powder and sterile liquid (Immuno-VIP) for oral consumption, or as creams, mouth - washing liquid or intimate hygiene products (Immuno-CIP).

The oral and local application of Immuno-VIP and Immuno-CIP products may be done after establishing the diagnosis and laboratory confirmation on antibiotic resistance.

Immuno-CIP product may be used in combination with pharmaceutical products with dedicated purpose. For visible effects it is advised the product application at least twice a day (in the morning and in the evening).

Immuno-VIP may be used as supplement both for adults (one teaspoon of approx. 5g, daily) and children over 6 months (½ spoonful of approx. 2.5g, daily). The granules should be blended in a glass of liquid (water, juice, tea, milk, etc.) at room temperature. The liquid is then ingested by mouth washing, sipping and gargling.

Local application can be repeated several times during the day, depending on the skin reaction. The natural egg white analgesic effect is preserved for about 5 hours.

In case of urinary infections, with skin irritation in the genital area, is recommended to apply Immuno-CIP liquid product, after the affected area is clean and dry. Local application is mandatory associated with oral use of Immuno-CIP.

After the amelioration of skin and mucous membranes lesions it is recommended to continue the oral and local application for more 10-12 days.

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