Cancer Association of South Africa (CANSA)

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Fact Sheet on Antibiotic Resistance and Cancer Treatment

Introduction

Antibiotic resistance is one of the most serious health threats currently faced by the world. Infections from resistant bacteria are now too common, and some pathogens have even become resistant to multiple types or classes of antibiotics (antimicrobials used to treat bacterial infections).

[Picture Credit: Antibiotics I]

The loss of effective antibiotics will undermine the ability to fight infectious diseases and manage the infectious complications common in vulnerable patients undergoing chemotherapy for cancer, dialysis for renal failure, and surgery, especially organ transplantation, for which the ability to treat secondary infections is crucial.

When first-line and then second-line antibiotic treatment options are limited by resistance or are unavailable, healthcare providers are forced to use antibiotics that may be more toxic to patients and frequently more expensive and less effective. Even when alternative treatments exist, research has shown that patients with resistant infections are often much more likely to die, and survivors have significantly longer hospital stays, delayed recuperation, and long-term disability.

Efforts to prevent such threats build on the foundation of proven public health strategies: immunisation, infection control, protecting the food supply, antibiotic stewardship, and reducing person-to-person spread through screening, treatment and education.
(Frieden, 2013).

Key Facts Around Antibiotic Resistance

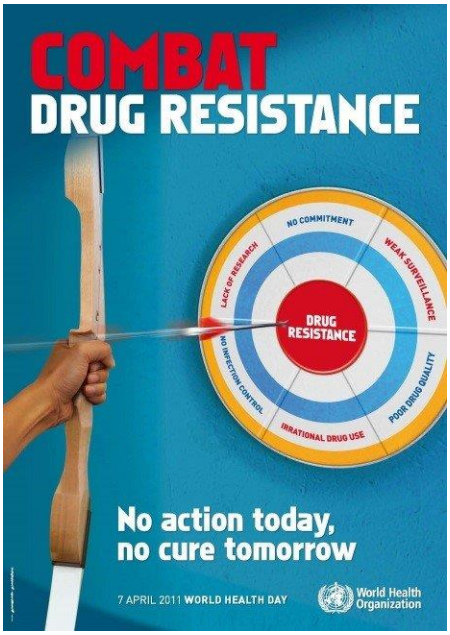
The World Health Organization released the following key facts around antibiotic resistance during April 2015:

- Antimicrobial resistance threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi.

- It is an increasingly serious threat to global public health that requires action across all government sectors and society.

- Antimicrobial resistance is present in all parts of the world. New resistance mechanisms emerge and spread globally.

- In 2012, WHO reported a gradual increase in resistance to HIV drugs, albeit not reaching critical levels. Since then, further increases in resistance to first-line treatment drugs were reported, which might require using more expensive drugs in the near future.



[Picture Credit: Combat Drug Resistance]

- In 2013, there were about 480 000 new cases of multidrug-resistant tuberculosis (MDR-TB). Extensively drug-resistant tuberculosis (XDR-TB) has been identified in 100 countries. MDR-TB requires treatment courses that are much longer and less effective than those for non-resistant TB.

- There are high proportions of antibiotic resistance in bacteria that cause common infections (e.g. urinary tract infections, pneumonia, bloodstream infections) in all regions of the world. A high percentage of hospital-acquired infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus*(MRSA) or multidrug-resistant Gram-negative bacteria.

- Treatment failures due to resistance to treatments of last resort for gonorrhoea (third-generation cephalosporins) have been reported from 10 countries. Gonorrhoea may soon become untreatable as no vaccines or new drugs are in development.

- Patients with infections caused by drug-resistant bacteria are generally at increased risk of worse clinical outcomes and death, and consume more health-care resources than patients infected with the same bacteria that are not resistant.

(World Health Organization, 2015).

Antibiotic Resistance: the Facts of 2017

A major menace looms. In 2017, many more people could begin dying from common bacterial infections. As resistance to antibiotics booms, diseases from gonorrhoea to urinary tract infections are becoming untreatable – a situation that looks set to get worse as the world reaches a new tipping point.

The world is about to reach the point where more antibiotics will be consumed by farm animals worldwide than by humans. This will mean more resistant bacteria, which could be a big threat. The livestock industry has long played down any risk to human health caused by using antibiotics in farming, but the danger is now accepted, according to the UN Food and Agriculture Organization (FAO).

Colistin, a drug that is used more often in animals than people, is one example. It is now the only antibiotic left that works against some human infections, yet colistin resistance has developed, and spread worldwide in 2015. The European Medicines Agency says bacteria resistant to colistin probably arose in livestock, and that some EU countries could easily cut their use of this antibiotic 25-fold.

The UN General Assembly has called for countries to encourage the best use of antibiotics. But it hasn't yet called for specific measures, such as banning their use to assist livestock growth – rather than fight infections – which can promote resistance.
(New Scientist).

Very Few Antimicrobial and Antibiotic Drugs Being Developed

The golden era of antibiotics began with the discovery of penicillin in 1928. From then into the 1970s, 270 drugs were developed to ward off infections, ushering in the age of modern medicine. Business was booming and by 1990, 18 of the world's largest pharmaceutical companies manufactured and sold antibiotics, according to a 2011 study by economists Adrian Towse and Priya Sharma published in the International Journal of the Economics of Business.

Then interest began to drop off. By 1991, half of the drug manufacturers had cut funding for fighting infectious diseases from the 1970s levels. A decade later, major companies abandoned antibiotics altogether. Today, only six of the top 50 pharmaceutical companies, as ranked by sales, are still pursuing antibiotic research.
(International Business Times).

According to Dame Sally Davies, the world has not seen a new class of antibiotics since the late 1980s and there are very few antibiotics in the pipeline of the big pharmaceutical companies that develop and make drugs. Pointing to the perceived unprofitability of developing new antibiotics, she called on new ways to incentivise the pharmaceutical industry to develop innovative new antibiotics.
(The Institute for Cancer Research).

[Picture Credit: Antibiotics II]

According to Dr Joseph R Dalovisio, President of the Infectious Diseases Society of America, health providers are running short on ammunition in their battle against antibiotic-resistant infections and experts warn that the lack of investment in antibiotic research and development could cost many individuals their health.

There simply aren't enough new drugs in the pharmaceutical pipeline to keep pace with the evolution of drug-resistant bacteria, the so-called 'superbugs'.

Out of the 506 new drugs currently in development, only five are new antibiotics. Two years ago, out of the 89 new medications that emerged, not one was an antibiotic, Dalovisio said.

Major pharmaceutical companies have abandoned or cut back antibiotic research and development. Because antibiotics work so fast and so well, the drugs reap weak returns on investments for manufacturers. More companies invest in long-term drugs for the treatment of chronic illnesses, such as insulin for diabetes, which can be taken for a lifetime. Evolving

bacteria that resist drugs make antibiotics less effective to the patient and less profitable to the manufacturing company in the long term.
(MedScape Multispeciality).

The Importance of Antibiotics Drugs

Antibiotics and antimicrobials are integral to modern health care and have enabled the use of invasive surgical or immunosuppressive medical procedures that depend on the ability to keep the body free of infection. Prophylactic antibiotics are used routinely as part of surgery, organ transplantation, and cancer chemotherapy to prevent infections.

Increasing antibiotic resistance threatens the efficacy of these procedures and could result in adverse clinical outcomes, including increased rates of morbidity, amputation, or death.

In addition to making the treatment of patients with infections difficult, antibiotic resistance also limits the efficacy of antibiotic prophylaxis, leading to worse outcomes in patients undergoing surgical procedures or receiving immunosuppressive cancer chemotherapy.
(Teillant, *et al*.|).

Antibiotic Resistance and Treatment of Cancer Patients

Bacterial infection is one of the most frequent complications in cancer patients and haematopoietic stem cell transplant recipients. In recent years, the emergence of antimicrobial resistance has become a significant problem worldwide, and cancer patients are among those affected. This poses a major threat to human health – antibiotics are the main line of defence when one's immune system is overwhelmed by bacteria. Bacterial infections can affect anyone, but the old, the young, the sick, and cancer patients are particularly vulnerable.
The lowering of immune defences can sometimes be life threatening for cancer patients. It also puts a great strain on the health system. Picking up an infection is the main cause of hospitalisation during chemotherapy treatment. It is said that as many as one in five cancer patients undergoing treatment are hospitalised due to infection.

If it is anticipated that a certain cancer treatment will make a person's immune system dangerously low, pre-emptive antibiotics are given to them to reduce their risk of getting infections. The trouble with this approach is that the more antibiotics are used, the more the growth of hardier strains of germs are favoured – this is but one of the areas where antibiotic resistance comes from.

Treatment of infections due to multidrug-resistant (MDR) bacteria represents a clinical challenge, especially in the case of Gram-negative bacilli, since the therapeutic options are often very limited. As the antibiotics active against MDR bacteria present several disadvantages (limited clinical experience, higher incidence of adverse effects, and less knowledge of the pharmacokinetics of the drug), a thorough acquaintance with the main characteristics of these drugs is mandatory in order to provide safe treatment to cancer patients with MDR bacterial infections. Nevertheless, the implementation of antibiotic stewardship programmes and infection control measures is the cornerstone for controlling the development and spread of these MDR pathogens.
(Gudiol & Carratalà, 2014).

For more than half a century, antibiotic drugs have ensured that potentially life-threatening bacterial infections were treatable. Today, however, more and more bacterial infections fail to respond to antibiotic treatment. Antibiotic resistance is a growing menace to all people and if nothing is done, treatments for common infections will become increasingly limited and expensive - and, in some cases, non-existent.

Antibiotic resistance poses a threat to everyone, but cancer patients are at particular risk. Cancer is typically treated with surgery, radiation, chemotherapy, and/or transplantation of bone marrow or blood stem cells. Each of these treatment techniques leaves a patient more vulnerable to infection than a healthy person of similar age.

Cancer treatments increase the risk of getting an infection, so antibiotics are an essential part of treating cancer patients. Many cancer patients need antibiotics during all stages of their treatment.

Surgery	**Radiotherapy**	**Chemotherapy**
Usually used to remove tumours. At least 5% of patients develop an infection. Infections can cause pain, longer hospital stays, and longer recovery time. Infections can make cancer treatments less successful.	Used to kill cancer cells, but can damage nearby healthy cells. Cells in hair, skin, and mouth and gut linings are most affected by this. Loss of these protecting cells increase the risk of getting an infection for which an antibiotic would be needed.	Used to stop the growth of cancer cells. Weakens the immune system and increases the risk of getting an infection. Infections can get worse quickly and cause severe illness. Infections can delay further chemotherapy sessions and make cancer treatment less successful
Antibiotics are crucial for controlling these infections and improving survival rates.		

Most cancer patients will need antibiotics to survive. Antibiotic resistance means that current antibiotics may not work. In addition, very few new treatments are being developed. This means that cancer survival rates may decrease because doctors might not be able to control infections.
(Antibiotic Action).

<u>Surgery as a treatment option for cancer</u> – Major surgery puts a great strain on the body, as well as leaving wounds which can harbour infection. There is a more general effect on the immune response as well, leaving people vulnerable to bacteria and in need of effective antibiotics and antimicrobials.

A large majority of cancer patients undergo surgery. Infections at the site of surgery account for approximately 40% of all infections in surgical patients. Many of these surgery-related infections are bacterial, and growing numbers of them are resistant to multiple antibiotics.

<u>Radiation therapy as a treatment option for cancer</u> - another cancer treatment is radiation, which is often used in combination with other types of therapy. Unfortunately, radiation is not selective and destroys all cells in its pathway, including those necessary to ward off disease.

A patient who undergoes radiation treatment for head and neck cancer, for example, may end up with ulcers in the mouth, which breaks down the mouth's protective barrier and leaves it vulnerable to invasion by harmful bacteria which usually necessitate the use of effective antibiotics and antimicrobials.

Chemotherapy as a treatment option for cancer - chemotherapy, or the administration of drugs to kill cancer cells, is the treatment mainstay for cancer that has metastasised, or has spread, beyond the originating site.

Chemotherapy, also, can help reduce pain associated with incurable cancers. As with radiation, all but the newest chemotherapy drugs are nonspecific in their target and destroy many other cells that are necessary to the immune system.

There are two very common consequences of chemotherapy. One is the destruction of white blood cells that are required to fight off bacterial infection. The other is severe damage and inflammation of the lining of the mouth, gastrointestinal and respiratory tracts - leaving an easy gateway for disease-causing bacteria to enter the body.

The availability of effective antibiotics in cases like this can be lifesaving.

Bone marrow transplantation as a treatment option for cancer - transplantation of bone marrow or blood stem cells has become a standard therapy for patients who require high doses of chemotherapy. The procedure requires removal and storage of the patient's marrow or stem cells (or that of a matched donor) before chemotherapy is initiated, because chemotherapy causes prolonged suppression of the bone marrow's ability to form new disease-fighting cells.

Once chemotherapy is concluded, the patient's marrow or stem cells can then be returned to the patient. But while intensive chemotherapy is underway and before the marrow has resumed normal function, infection is a major cause of mortality.

During the first month or two after the transplant, effective antibiotics are a mainstay of treatment and necessary for the patient's survival. Antibiotics have revolutionised cancer treatment by enabling the use of more aggressive therapies. This has led to dramatically higher survival rates.

One of every eight men and one of every nine women in South Africa is expected to develop cancer during their lifetimes, and many of them will be treated with one or more of the therapies described above. For this medically vulnerable group - and for society as a whole - the loss of effective antibiotics would have immense ramifications.

Although careful use of antibiotics can result in the emergence of antibiotic-resistant bacteria, inappropriate use greatly accelerates this process. The more often bacteria are exposed to antibiotics, the more resistant they become. Because bacteria reproduce rapidly, these antibiotic-resistant bacteria can spread efficiently. Unlike higher organisms, bacteria can transfer DNA to other bacteria that are not their offspring, and even to members of completely unrelated bacterial species. In effect, bacteria can teach one another how to outwit antibiotics.
(Keep Antibiotics Working; Longitude Prize).

Antibiotic-Resistant Gram-Negative Bacterial Infections in Patients With Cancer
A dramatic evolution has recently occurred in the significance of infections caused by gram-negative bacteria. Decades of progress in the care of patients with cancer, concomitant to the development of safe and effective antimicrobials, are being undermined. Patients with cancer, particularly those with hematologic malignancies, remain exquisitely vulnerable to infection with gram-negative bacteria as a result of neutropenia, lymphocyte dysfunction, mucositis, and the use of invasive devices. At the same time, the effectiveness of our current prophylactic and empiric antibiotic regimens is compromised by the emergence of gram-negative bacteria that exhibit multidrug-resistant (MDR), extensively drug-resistant (XDR), and pandrug-resistant (PDR) phenotypes. This trend is exacerbated by the successful global dissemination of “high-risk clones” of MDR gram-negative bacteria].

At the present time, clinicians struggle to devise effective guidelines that assist with the choice of therapy for infections caused by antibiotic resistant gram-negative bacteria in cancer patients.

Presently, the implementation of effective antimicrobial stewardship and infection control programs remains essential. Regardless of how these practices develop and how the landscape of antimicrobial resistance evolves, we anticipate that fundamental lessons on how to treat gram-negative bacterial infections will continue to be learned from patients with cancer and neutropenia.
(Perez, Adachi & Bonomo).

You Can, I Can

There is not something which everyone **CAN** do
There is actually something that everyone **MUST** do

And that is:

Do not ask, and do not expect, antibiotics for colds, sore throats, or flu

Colds, sore throats, and flu are caused by viruses and antibiotics do not work

Only take antibiotics prescribed by a doctor

Use antibiotics EXACTLY as prescribed on the container

Always complete the full course of antibiotics

Never give or share antibiotics with others

The good news is that by doing something very simple
everyone can do something very good -
everyone can, in a very concrete way help cancer patients,
now and into the future

Medical Disclaimer

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