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Antimicrobial resistance –

Why diagnostics play a crucial role in addressing a global challenge.

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Abstract

As recognized by the World Health Organization (WHO), antimicrobial resistance (AMR) is a major global health threat. impacting our ability to effectively treat infectious diseases.

The impact of AMR is profound, with over 700,000 deaths annually attributed to drug-resistant infections, a number expected to reach ten million by 2050. Common infections become increasingly difficult to treat due to the prevalence of AMR strains.

The paper discusses various diagnostic tools available for different types of infections. By adopting appropriate tests and responsible antibiotic practices, we can contribute to the global efforts to combat AMR and safeguard public health.

Antimicrobial resistance: a global multifaceted phenomenon

Antimicrobial resistance (AMR) is according to WHO* one of the top 10 global public health threats which significantly impacts our ability to treat infectious diseases. Misuse, taking antibiotics for colds and other viral illnesses doesn't work - and it can create bacteria that are harder to kill. Taking antibiotics too often or for the wrong reasons can change bacteria so that antibiotics no longer work against them. The overuse of antibiotics combined with natural adaptive capabilities of microorganisms have led to the rise of multi-resistant gram-negative bacteria (MRGNs).

The impact of AMR

Even in Western countries, 30% of antibiotic prescriptions are considered either unnecessary or suboptimal.[1] Overprescribing and uncontrolled use of antibiotics in agriculture lead to antimicrobial resistance (AMR). Common infections become untreatable due to the emergence of AMR. More than 700,000 people die each year from drug-resistant infections, and this number is expected to reach ten million by 2050. [2]

The role of Diagnostic testing

Effective diagnostic testing plays a pivotal role in addressing AMR. During WHO's presentation of the Essential Diagnostic List (EDL-3), Dr. Hanan Balkhy** emphasized the importance of antimicrobial resistance (AMR). She said AMR is a silent pandemic, made even more important by COVID-19, as funding for general diagnostics has been reduced, yet more antibiotics have been prescribed. She mentioned that c-reactive protein (CRP), procalcitonin (PCT), and other parameters play an important role and it should be the rule in every country: "diagnosis before prescription" of antibiotics. And more and more parameters will be mentioned in the EDL that will have this focus, she concluded. Therefore, we should all make AMR a recurring theme in our sales conversations with customers.

Current landscape of diagnostic testing

A recent report on antimicrobial resistance[3] calls for testing to identify viral and bacterial infections. Only bacterial infections respond to antibiotics. The review team says such tests could end "just in case" prescribing, in which a large proportion of antibiotics are used unnecessarily. According to the report, some rapid diagnostic tests already exist that can reduce antibiotic prescribing.

Therefore, it is crucial to distinguish between bacterial and viral infection, as only bacterial infections respond to antibiotics.

For example, blood tests for C-reactive protein (CRP) can give an indication of whether an infection is likely bacterial. Although such tests are not perfect, they have been widely used for years in the Netherlands and Scandinavia, which have some of the lowest antibiotic prescription rates in Europe. C-reactive protein (CRP) is widely used as a biomarker for the presence of an inflammatory process and is the most extensively studied marker for distinguishing bacterial from nonbacterial infections in febrile patients. The literature reviewed suggests that CRP testing may be beneficial in resource limited settings to improve the rational use of antibiotics in febrile patients.[4] CRP can be determined qualitatively with a simple RDT and quantitatively with a test on lateral flow system, such as **HumaFIA** (REF 16090/20), or on a clinical chemistry analyzer. (See HUMAN REF 40040/40042 and REF 11141/11241/11241300/1241600 respectively).

Procalcitonin (PCT), another biomarker positive for bacterial infection and sepsis is becoming increasingly popular. PCT is often said to be superior to CRP and more specific for sepsis and bacterial infections. This is because PCT begins to rise earlier and returns to normal concentration more quickly than CRP, allowing earlier diagnosis and better monitoring of disease progression[5] (HUMAN offers PCT on **HumaCLIA**, REF 85820 and on **HumaFIA**, REF 16090/25).

White blood cells (WBC) and neutrophils

C-reactive protein (CRP), and White blood cell count (WBC) are often part of the diagnostic workup in an inpatient setting. Neutrophils are infection fighters that increase during bacterial infections. Lymphocytes, on the other hand, can increase in cases of viral infections. The percentage of neutrophils compared to a total WBC count is reported to be better at discrimination viral from bacterial infection. The lack of rise in neutrophil count correlates well with viral cases.[6] The hematology line of HUMAN provides an ideal instrument, the **HumaCount 5D^{CRP}**, since it differentiates the WBC and offers CRP from the same sample (REF 16451)

Urine diagnostic

Worldwide, urinary tract infections (UTI) are among the most common bacterial infections: Approximately 150 million people are affected annually.[7] Even so, 83% of these patients may not require any urinalysis testing before getting an antibiotic prescription.[8] Suspected UTIs contribute to high laboratory workloads, with up to 80% of specimens ultimately negative.[9]

As a result, many patients unnecessarily receive empiric treatment with broad-spectrum antibiotics, fueling the rise of antibiotic resistance.[8] The test strip is the most common **rapid test** for urinary tract infection. (See HUMAN REF 22132 and 23111).

Antibiotic susceptibility testing (AST)

While traditional culture-based methods remain important for identifying pathogens, they are time-consuming and may delay appropriate treatment decisions. To overcome several rapid diagnostic technologies have been developed.

The European Centre for Disease Prevention and Control (ECDC) has estimated that to date 30–50% of all antimicrobials prescribed to human patients are unnecessary[10], and over-prescription of antimicrobials further promotes the development and spread of resistance.

AST provides an in vitro measure of bacterial response to an antimicrobial agent that predicts therapeutic efficacy. Standard AST methods require isolated organisms and effectively take a day to perform. Most common are urine and blood culture.

AST can also help to identify isolates with defined resistance mechanisms of major interest to infection prevention and control (for example, extended-spectrum β-lactamase producers, carbapenemase-producing Enterobacteriaceae, methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci).[10]

Summary and key facts according to WHO[11]:

- Antibiotic resistance can affect anyone of any age and in any country.
- Antibiotic resistance occurs naturally, but misuse of antibiotics in humans and animals accelerates the process.
- Antibiotic resistance is now one of the greatest threats to global health, food security and development.
- A growing number of infections - such as pneumonia, tuberculosis, gonorrhea, and salmonellosis - are increasingly difficult to treat because the antibiotics used to treat them are becoming less effective.
- Antibiotic resistance leads to longer hospital stays, higher medical costs, and increased mortality.

It is not inconceivable that one day medical procedures such as organ transplants, cancer chemotherapy, diabetes treatment, C-sections, and hip replacements will be considered very high risk - and that the risk of dying from a common infection will outweigh the benefits of the medical procedure.

It's not enough to develop new drugs. The discovery of new antimicrobials is too slow to keep up with how quickly microbes evolve to become resistant to old drugs.[2] We need to maintain the effectiveness of the antimicrobials we currently have. It is equally important that we move away from broad overprescribing of antibiotics to more targeted therapy.

Conclusion and outlook

Diagnostics enable optimal use of existing medications and protection of new treatments. A simple diagnostic test that indicates the presence or absence of a bacterial infection can dramatically reduce the overuse of antibiotics. Please make use of the products HUMAN offers to fight against AMR.

Follow us on **social media** for updates and use the **hashtag** #AMRfighter when sharing! We look forward to your comments and discussion on the topic. Any request for further information? – Contact the author of this paper, **Dr. Alfons Krug** at a.krug@human.de

References

[1] Centers for Disease Control Prevention. *Be Antibiotics Aware: Smart Use, Best Care | Features | CDC*. Available online (Centers for Disease Control Prevention, last reviewed in November 2021) at: https://www.cdc.gov/patientsafety/features/be-antibiotics-aware.html (accessed July 7, 2023).
[2] United Nations meeting on antimicrobial resistance. *Bull World Health Organ. 2016 Sep 1; 94(9):638-639.*
[3] https://www.bbc.com/news/health-34607822 (accessed July 11, 2023)
[4] http://dx.doi.org/10.1136/bmjgh-2020-002396
[5] Meisner M. Procalitonin: Experience with a new diagnostic tool for bacterial infection and systemic inflammation. J Lab Med 1999; 23:263-72
[6] Elemraid MA, Rushton SP, Thomas MF, Spencer DA, Gennery AR, Clark JE. Utility of inflammatory markers in predicting the aetiology of pneumonia in children. Diagn Microbiol Infect Dis [Internet]. 2014;79(4):458–62.
[7] Stamm WE, Norrby SR (2001): Urinary tract infections: Disease paranormal and challenges. J Infect Dis 183 (Suppl.1) S1-S4.
[8] Pujades-Rodrigues M. et. al (2019): Lower urinary tract infections: management outcomes and risk factors for antibiotic re-prescription in primary care. EClinicalMedicine. Volume 14, P23-31, September 2019, DOI: https://doi.org/10.1016/j.eclinm.2019.07.012
[9] Keller, P. (2019): Ein neuer Schritt zur schnelleren Urinanalytik (in German)
[10] van Belkum, A., Bachmann, T.T., Lüdke, G. *et al.* Developmental roadmap for antimicrobial susceptibility testing systems. *Nat Rev Microbiol* **17**, 51–62 (2019). https://doi.org/10.1038/s41579-018-0098-9
[11] WHO. Factsheets, Antibiotic resistance, 31 July 2020: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance (accessed July 7, 2023).

* https://openwho.org/channels/amr
** Biography (WHO) of Dr. Hanan Balkhy: https://www.who.int/director-general/who-headquarters-leadership-team

About HUMAN

Founded in 1972, HUMAN has been one of the global players in the IVD industry for more than 50 years.

Its broad and steadily growing portfolio ranges from classical clinical chemistry to innovative molecular diagnostic methods as well as special applications like assays for autoimmunity testing. With its worldwide service and delivery capacities and a broad network of long-standing distributors, HUMAN supports medical laboratories in over 160 countries and is a recognized partner to numerous governmental and non-governmental organizations.

HUMAN has its headquarters in Wiesbaden, Germany, and maintains regional sales offices in the United Arab Emirates, Singapore, China, India, Panama. It has local HUMAN representatives in many other countries.

Sustainability is a particular concern for HUMAN as a responsible and future-oriented company. A certified environmental management system has been established that meets the requirements of the international ISO 14001 standard and the European EMAS directive.