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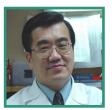
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Since 1983, the APUA Newsletter has been a continuous source of non-commercial information disseminated without charge to healthcare practitioners, researchers, and policymakers worldwide. The Newsletter carries up-to-date scientific and clinical information on prudent antibiotic use, antibiotic access and effectiveness, and management of antibiotic resistance. The publication is distributed to over 7,000 affiliated individuals in more than 100 countries. The material provided by APUA is designed for educational purposes only and should not be used or taken as medical advice. We encourage distribution with appropriate attribution to APUA. See previous editions of the Newsletter on the APUA website.

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APUA Newsletter Vol 38, No 1.



Jean Carlet
President

The key role of non-profit nongovernmental organisations (NGO) in the fight against antibiotic resistance: the example of WAAAR

Jean Carlet and Garance Upham on behalf of the WAAAR Executive Committee



Garance Upham Vice-President

The role of non-governmental organisations (NGOs) has been key for many diseases in the past. Such is the case for antimicrobial resistance (AMR), which nowadays represents a very serious and worldwide public health threat. Associations like APUA, ReAct and the <u>World Alliance Against Antibiotic Resistance (WAAAR)</u> are devoted to the continuous fight against AMR.

This article will look at the example of WAAAR, created in 2011, which has undertaken many initiatives. Initially set up in France, WAAAR has been very successful in communicating with politicians and health deciders in order to bring their attention to the topic of AMR. They became anxious when they saw the sharp increase in

E.coli resistance to cephalosporins, and the high number of deaths and the costs associated with AMR. In a worldwide competition within the European Union, WAAAR came in third place, behind two NGOs which are mostly active on animal health.

Strong programmes, which have been in place in France since 2000, programmes in this area."
have been reinforced, in particular

for surveillance of AMR, in close cooperation with the European Centre for Disease Prevention and Control (ECDC). In 2014, WAAAR organised a worldwide declaration on AMR which has been widely disseminated and very successful. A very informative newsletter, AMR-Times, was established, as well as a yearly publication—AMR Control. AMR Control has seen the highest level of participation including an introduction by WHO Director-General, Dr Tedros, in 2018, UN Interagency Coordination on Antimicrobial Resistance Group in 2019 and the participation of many key players and countries, from CARB-X to China, Germany, Japan, Senegal, Switzerland, the USA Centre for Disease Control and Prevention (CDC) and Biomedical Advanced Research and Development Authority (BARDA) to name a few. Articles can be downloaded at www.amrcontrol.info

Presently, the association gathers more than 750 people from 60 different countries belonging to all continents. Since the creation of WAAAR, we decided to set up a multi-disciplinary Executive Committee with clinicians (in particular ID people), microbiologists, intensivists, infection control specialists, veterinarians, non-medical members very active in the field of AMR and members of consumer organisations. We always considered that the multi-disciplinary case-mix of the Executive Committee is key for the efficacy of the various NGOs in the field of AMR.

In the last few years, we have participated in many activities and working groups—in particular with WHO,

the United Nations and ESCMID to name only a few. The cooperation with European scientific societies has become stronger and stronger. To give an example, WAAAR has been involved with ESICM and ESCMID in a scientific group devoted to the fight against AMR in the intensive care units (called Antarctica). A paper was published on this issue by the group², and an international prevalence study is

"Eighty per cent of antibiotic consumption comes from the community, and it is key to develop strong programmes in this area."

ongoing.

WAAAR is active in several important scientific and research programmes, such as EU-AMRAI, JAMRAI and EUCIC — the latest being a large European group organised by ESCMID that works on infection control, healthcare-associated infections and AMR.

In the two last years, we have developed a large communication programme targeting politicians, people from the National Assembly and the Senate, as well as VIPs from each region, and mayors.

Eighty per cent of antibiotic consumption comes from the community, and it is key to develop strong programmes in this area. Cooperation with GPs has been very weak in the past, and the participation of GPs in national working groups and task forces has been

minimal for several reasons—in particular their very dense agenda. We will organise the main structures representing general practice, including several action syndicates and a national communication, information and education. This programme must be decided and driven by GPs themselves since, at least in France, they dislike drastic top down measures coming from politicians and paymasters. To initiate the campaign, many top French experts came together to publish "A Policy to Combat Antibiotic Resistance - An Implementation Manual". The key document has been translated into English and became a hot item at the United Nations World Health Assembly and other meetings, in both French and English!

There are many projects planned for the future. WAAAR intends to facilitate the fight against AMR in low- and middle- income countries, particularly African ones, in cooperation with WHO and many players such as the Merieux Foundation, the Wellcome Trust and Médecins Sans Frontières (Doctors without Borders). Stronger cooperation with East European countries (such as Russia), India and China is also necessary. There are already some actions ongoing with those countries.

Finally, we think that important and long-term actions and programmes should be developed, coming from strong cooperation of the main NGOs. This never really happened in the past, mostly due to the competition between these. We think however, that cooperation between NGOs such as APUA / ISAC, ReAct and international consumer organisations would be synergistic and stronger—particularly in lobbying politicians, national European or international deciders and the public. Joint sessions could also be proposed to the large scientific societies.

References

- 1. Carlet J et *al.* French national program for prevention of healthcare-associated infections and antimicrobial resistance, 1992-2008: positive trends, but perseverance needed. French National Program for Prevention of Healthcare-Associated Infections and Antimicrobial Resistance. *Infect Control Hosp Epidemiol*. 2009;8:737-45
- 2. De Waele J *et al.* Antimicrobial resistance and antibiotic stewardship programs in the ICU: insistence and persistence in the fight against resistance. A position statement from ESICM/ESCMID/WAAAR round table on multi-drug resistance. *Intens Care Med.* 2017;44:189-196



International Centre for Antimicrobial Resistance Solutions (ICARS)

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Robert Skov Scientific Director



Ghada Zoubiane Independent Consultanat

to

evidence



the

Kåre Mølbak Founder

and

development

The increasing problem of antimicrobial resistance (AMR) has long been recognised by researchers and professionals both in human and veterinary medicine, but has only recently been more generally acknowledged. In the last five years, several reports 1,2,3,4 have highlighted the global crisis of AMR and WHO has ranked it among the top 10 most serious medical problems. Yet, as urgently highlighted in the final report of the UN Inter-Agency Co-ordination Group (IACG)⁵ on AMR, the global response does not sufficiently match the scale and scope of the issue and challenges remain in implementation, particularly in low- and middle-Income countries (LMICs). Over 140 nations have developed, or are currently developing, a National Action Plan (NAP) against AMR. However, executing these plans is not straight forward because at times, those creating the solutions are part of the problem.

In response to this challenge, Denmark, with support from the World Bank, has taken the initiative to

the establish International Centre for Antimicrobial Resistance Solutions (ICARS) - a partnership that focuses on co-developing intervention and implementation research with LMICs. It is envisaged that ICARS will be an international 'One Health' knowledge, intervention and implementation research partnership; a platform for generating, assessing and using implementation of cost-effective and context-specific solutions to AMR in LMICs. Doing so, ICARS will expedite action by translating policy into practice.

support

ICARS will work at both a national and an international level and work out of five core principles (see **Table**).

At a national level, ICARS will partner with governments of LMICs to support the translation of NAPS by supporting evidence-based solutions using a one health approach. ICARS will work with the country's AMR Coordinating Committees and other stakeholders to identify and prioritise activities. Projects will be developed in partnership with local research institutes taking a cross- and transdisciplinary approach, national and local policymakers, professionals, businesses, communities, and wider stakeholders (the Tripartite, United Nations Environment Programme [UNEP], nongovernment organisations [NGOs], amongst others) as

Country Ownership	Country led Priorities defined by individual countries based on country NAPs, needs and challenges at national and local levels Integrated top down (e.g. government, local authorities) and bottom up (e.g. professionals, academia, community representatives) approach in country
One Health	A collaborative, multisector and holistic approach Actions relevant to human and animal health, the environment, global food security and economic prosperity AMR specific and AMR sensitive activities
Partnership	A solution development partnership - delivering in partnership with key stakeholders at various levels (international, regional, national, and/or local) Alignment and collaboration across public, private, and philanthropic sectors and various disciplines Maximising the use of limited resources, building on existing work for an effective approach and to avoid duplication Participatory cross-disciplinary research approach
Solution-Focused	 Focusing on providing policy relevant evidence-based solutions Translation of country NAPs and international policies, standards and frameworks into practice on the ground Identifying causes and barriers to implementation of existing solutions Combining immediate action with long-term vision
Sustainability	 Cost-effective solutions (economically feasible and practical for the country) Laying the foundations for change and supporting initial implementation Integrating into existing resources, systems and infrastructure, where possible Capacity and capability building in country – supporting leaders and local champions, utilising and expanding expertise of existing capacity and training the next generation Alignment to other global and country agendas and priorities (e.g. SDGs, Universal Health Coverage)
Table: Core Principles of ICARS	

appropriate (see **Figure**). By close consultation, collaboration and alignment with existing activities, ICARS will avoid duplication, build on, and strengthen the essential wider efforts to address AMR within the country. Projects will include economic evaluations to inform of the cost-benefit of the identified solutions. Output from these projects will be owned by the countries and ICARS will work to make data as

accessible as possible to the wider global community.

At an international level, and anchored by hubs with projects and activities in various locations around the world, ICARS will play a key role in the delivery of the UN General Resolution Assembly **AMR** agreed in September 2016, the Global Action Plan and international strategies and agendas. ICARS will do so by of filling some the gaps highlighted the **IACG** in recommendations⁵ calling for independent evidence

synthesis, reports on the science and evidence related to AMR, its impacts and future risks, and recommendations for adaptation and mitigation. Outputs will be communicated to different stakeholders to increase awareness, and advocate for action.

Organisation

ICARS is currently embedded within the Danish government but during 2020, ICARS will transition into an independent organisation with clear governance and structure, attracting support and funding from other donors. The governance model for ICARS is envisaged to be structured around a Board of Trustees and relevant advisory forums, including a Stakeholder Forum, Scientific Advisory Forum and a Donor Forum.

Invitation to Participate

ICARS invites partnership from committed governmental bodies, policymakers, foundations and international organisations. This may take several forms, including political support and commitment, inkind contributions and/or financial contributions.

ICARS is working with LMIC partners who are committed to mitigating AMR and willing to show

leadership to initiate a number of demonstration projects in 2020, to identify and implement solutions to AMR. Supported projects will be continuously monitored, adapted, and evaluated while ICARS builds towards a larger and more long-term programme of work.

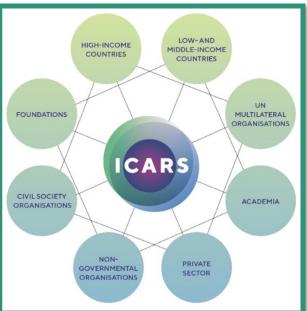


Figure. Stakeholders with whom ICARS wants to engage

References

1. O'Neill J. Tackling drugresistant infections globally:
final report and
recommendations. The
review on antimicrobial
resistance. Report. 2016

- 2. Jonas *et al* on behalf of World Bank Group. *Drug-resistant infections : a threat to our economic future* (Vol. 2): final report (English). HNP/Agriculture Global Antimicrobial Resistance Initiative. Washington, D.C. 2017
- 3. OECD. Stemming the superbug tide: just a few dollars more. OECD Health Policy Studies, OECD Publishing, Paris. 2018
- 4. Berthe, FCJ. et al, on behalf of the World Bank Group. Pulling Together to Beat Superbugs Knowledge and Implementation Gaps in Addressing Antimicrobial Resistance (English). HNP/Agriculture Global Antimicrobial Resistance Initiative. Washington, D.C. 2019
- 5. Interagency Coordinating Group on Antimicrobial Resistance. *No Time to Wait: securing the future from drug-resistant infections*. Report. 2019



From bad to worse: Emergence of extensively drug resistant Gram negative bacilli among Nigerian immunocompromised patients

Ibrahim Yusuf

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Humankind is beginning to lose the war against renewed threats posed by infectious agents and their resistance to available antibiotics. Previous mild infections are now turning into "monsters", killing hundreds of people globally with little or no options for cure. The number of affected patients in developing countries is higher than figures in developed nations to overuse of antibiotics, poor environmental pollution, poor infrastructure possible effects of the weather and climate in such nations⁸. Habits such as coughing in public places, discharge of sputum on bare floors, indiscriminate discharge of sewage in the environment, open defecation and urination has made infectious agents such as Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Salmonella spp. (which are often obtained and acquired in hospitals), readily

available on different environmental surfaces and has made dissemination of such bacteria much faster in the among community setting.

Isolation of different bacterial species as well as antibiotic resistant bacteria (ARB) from different clinical and environmental samples such as

restroom floors, door handles of rooms and schools, mobile phones, activated sludge, sewage, refuse dump sites, and also on vegetables, animals and humans has been documented in Nigeria^{2,12,13}. In the last decade, the prevalence has been increasing with no sign of respite. Of high concern is the alarming rate of Gramnegative bacilli (GNB), which are resistant to commonly prescribed and reserved antibiotics^{3,6,11}. The magnitude is so high now because of increasing isolation of multidrug resistant (MDR) GNB such as Escherichia coli, Klebsiella pneumoniae, Salmonella sp, Proteus sp etc that are resistant to last resort antibiotics that are not available for use in the community or healthcare facilities⁹.

Group and individual research findings in Nigeria have indicated beta lactamase production as the main cause of GNB resistance to penicillins, cephalosporins and carbapenems^{4,7,10}. However, routine microbiological laboratory investigations carried out in the majority of medical laboratories in Nigerian hospitals are not

capable of screening for or identifying specific beta lactamases produced by GNB or of isolating and characterising resistant Acinetobacter baumannii known to cause serious infections that are very hard to treat. By virtue of this, these pathogens are not being identified and this, in turn, leads to sub-optimal antibiotic therapy in Nigeria.

The category of patients most affected by these unidentified superbugs are hospitalised immunocompromised persons such as HIV infected individuals, children, elderly, pregnant women, diabetic patients, cancer patients, the malnourished and those on steroids and other immunosuppressive drugs. Concern about increasing morbidity, mortality, hospital stay, and severe economic loss to the patient and nation due to exhaustion of antibiotic options has been raised.

isolated from hospitalised immunocompromised patients, 22% exhibited an extensively drug resistant profile."

"Out of 68 Gram negative bacilli The latest results from a study carried out in a tertiary /referral hospital in the north western region of Nigeria showed a progression from **MDR** Extensively Drug Resistant (XDR) status among GNB⁵(Fig. 1). Out of isolated 68 **GNBs** from hospitalised

immunocompromised patients,

15 (22.1%) isolates exhibited an XDR profile. Conversely, no XDR was recovered from the hands of immunocompetent healthcare workers (HCW), but 5.9% of isolates from them were MDR. Preliminary investigation revealed that 53.3% of the XDR isolates from immunocompromised patients were ESBL producers, 13.3% were AmpC producers, 25% co-produced ESBL and AmpC and none of the isolates were phenotypically confirmed to be carbapenamase / metallo-beta lactamases (MBLs) producers. XDR Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes and Proteus mirabilis express 100% resistance Gentamicin, Piperacillin+Tazobactam, Aztreonam, Ceftriaxone, Amoxicillin, Amoxycillin/Clavulanic acid, Ciprofloxacin. Tetracycline and The organisms demonstrated a variable resistance pattern against meropenem, colistin and tigecycline.

Fifty percent of the XDR isolates were resistant to Colistin, 75% resistant to Tigecycline—leaving virtually no or very little antibiotics available for treatment.

Enterobacter aerogenes also demonstrated total Disease in Kano, Nigeria. Mediterr J Hematol Infect Dis. resistance to Meropenem, Cefoxitin and Tigecycline. Antibiotics with favourable activities against some of the XDR GNB in the study were Colistin, Tigecycline, Meropenem and combinations of Piperacillin-Tazobactam with either Ceftriaxone or Ceftazidime (Fig. 1).

Apart from behavioural factors such as selfmedication abuse of antibiotics, and anthropogenic factors, especially in Nigeria, that are believed to drive AMR from MDR to XDR status and facilitate their spread from one community / hospital to another, are: inappropriate antibiotic prescribing by community HCWs; unavailability of funds to engage in AMR research; non-communication of research findings to appropriate stakeholders; lack of implementation of suggestions from research adherence obsolete laboratory findings; to

procedures for investigation; of use multiple counterfeit sensitivity antibiotic questionable discs; practices in hospitals and health ministries; re-labelling/packaging of expired drugs; and persistent crisis between **HCWs** (especially doctors and medical laboratory scientists) over hospital unit leadership, which divert attention of HCWs away from patient safety.

2018;15;10

- 3. Ibrahim Y et al. Phenotypic Detection of Extended Spectrum Beta lactamase and Carbapenemase Coproducing Clinical Isolates from Two Tertiary Hospitals in Kano, North West Nigeria. Ethiop J Health Sci. 2017;27:3–10 4. Igbinosa E et al. Detection of Methicillin-Resistant Staphylococci Isolated from Food Producing Animals: A Public Health Implication. Vet Sci 2016;3:14.
- 5. Kankara, AS. Studies on Extensively Drug Resistant other Enterobacteriaceae amongst Immunocompromised Patients Attending Federal Medical Centre, Katsina. MSc Thesis, Department of Microbiology, Bayero University, Kano Nigeria. 2019
 - 6. Oli AN et al. Multi-antibiotic resistant extended-spectrum beta-lactamase producing bacteria pose a challenge to the effective treatment of wound and skin infections. Pan Afr Med. 2017;30;27:66
 - 7. Olowe O et al. Detection of bla CTX-M-15 extendedspectrum β-lactamase genes in Escherichia coli from hospital patients in Nigeria. Int J Antimicrob Agents

2010:35:206-207 8. Vikesland P et al. Differential Drivers of **Antimicrobial Resistance** across the World. Acc Chem Res. 2019:16;52:916 -924

9. Yusuf I et al. Emergence of carbapenem-resistant enterobacteriaceae in surgical and intensive care units of a hospital with low usage of carbapenem in Kano, North West Nigeria. Antimicrobial Resistance & Infection Control. 2013a:2;S1-P75 10. Yusuf I et al. Detection of multi drug resistant bacteria in major hospitals in Kano, North-West,

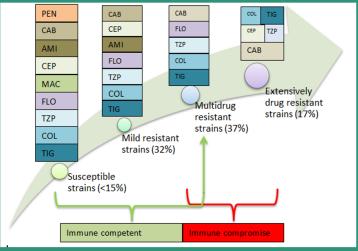


Fig. 1: Resistance pattern and available antibiotics for treating Gram negative bacilli isolated from immune compromised patients attending a Nigerian Federal Medical Center. Key: PEN=penicillins, CAB= carbapenems, AMI=aminoglycosides, CEP= cephalosporins, MAC=macrolides, FLO=flouroquinolones, TZP=Piperacillin-Tazobactam, COL=colistin, TIG=tigecycline

Despite efforts of organisations such as WHO, CDC, Nigeria. Brazilian J Microbiol. 2014;45:791-798 APUA and other non-governmental organisations in combating AMR globally, it seems Nigeria is far from reaching the milestone. Even though XDR pathogens were only detected among immunocompromised patients, other environmental, social, and economic factors could drive its dissemination to HCWs, other patients and other community members.

References

- 1. Chengula A, et al. Determination of bacterial load and antibiotic susceptibility testing of bacteria isolated from students' toilets at Sokoine University of Agriculture, Morogoro, Tanzania. Journal of Health, Medicine and Nursing. 2014;5: 1-11
- 2. Bello N et al. Characterization and Antimicrobial Susceptibility Profile of Bacteraemia Causing Pathogens Isolated from Febrile Children with and without Sickle Cell

- 11. Yusuf I et al. Prevalence and Antibiotic Susceptibility of Ampc And Esbl Producing Clinical Isolates At A Tertiary Health Care Center In Kano, North. African J Clin Exp Microbiol. 2013b;14:109-119
- 12. Mustapha A, et al. Detection of Multidrug-Resistance Gram-Negative Bacteria from Hospital Sewage in North East, Nigeria. Frontiers Envl Microbiol. 2019;5:1
- 13. Tsakul PA et al. Antibiotic susceptibility and plasmid profile of Escherichia coli from door handles in two tertiary institutions in Nasarawa State, Nigeria. J Adv Microbiol. 2017; 3:1-13

APUA Activities

APUA Symposium at ICC—GCCMID



APUA sponsored a symposium at the 31st International Congress of Antimicrobial Chemotherapy (ICC) — 4th Gulf Congress of Clinical Microbiology and Infectious Disease in Dubai in November 2019.

The symposium was very well attended. APUA Chair, Pierre Tattevin paid tribute to Prof. Stuart Levy and the following topics were presented:

- On the Threshold: Controlling MDROs by Antimicrobial Stewardship (Ian Gould).
- Controlling Multidrug-Resistant Gram-negative Bacilli: From Stewardship to Infection Control (Souha Kanj).
- How to Not Prescribe Antibiotics (Pierre Tattevin).

Stuart Levy Tribute Newsletter / Page

The APUA Editorial Team produced a special edition of the APUA newsletter to honour the memory of Prof. Stuart Levy, APUA founder and President, who sadly passed away in September 2019. Copies of the newsletter were distributed

at the ICC—GCCMID and were well received. Thank you to all who were able to contribute at such short notice.

You can read the newsletter here.

A tribute page has been set up on the APUA website with condolence messages from colleagues / friends of Stuart Levy. If you would like to add a message of your own, please email secretariat@ISAC.world

Updates to the APUA Board

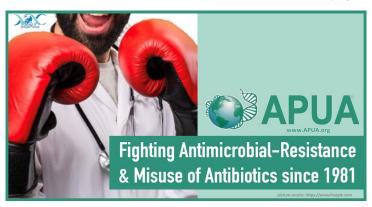
APUA is pleased to announce the addition of three new members to the Board:

- Ian Gould (UK)
- Po-Ren Hsueh (Taiwan)
- Heiman Wertheim (the Netherlands)

Unfortunately, Shahin Gharakhanian (USA) has stepped down from the Board.

Antibiotic Resistance Resources

APUA / ISAC is developing a website / repository of antimicrobial resistance (AMR) resources - visit the page.



If your institute, region or country is involved in tackling AMR, please share the link with secretariat@isac.world. Materials in all languages are welcome.

APUA Chapter News

APUA Russia

- New studies and phases of ongoing studies for 2020 including: PeHASus - Antibiotic resistance surveillance of the main pathogens causing upper RTIs (S. pneumoniae, H. influenzae, S. pyogenes); MARATHON Multicenter surveillance study on antimicrobial resistance of nosocomial pathogens; SPECTRUM - an Epidemiological, Microbiological survey to establish the spectrum of Circulating seroTypes of S.pneumoniae, in patients older 18 years: healthy Carriage, patients with non- • Graduate educational courses on bacteriology and clinical invasive and invasive pneumococcal infections in Russian Federation)
- In 2017, introduced Map of Antimicrobial Resistance of Russia, an interactive system for monitoring antibiotic resistance, • All-Russian educational project "Diagnosis, treatment, with tools for analysing and visualising data on the susceptibility of microorganisms to antibiotics. Updated in 2019.

2019 congresses

 XXI International Congresses on Antimicrobial Therapy APUA Nepal published its 16th newsletter which includes an (Moscow) - 1,253 participants

 Conference in Krasnodar (28-29 March 2019) and International Congress in Ufa (17-18 October 2019) - total 2757 participants

Planned activities / congresses

- XXII International Congresses on Antimicrobial Therapy in Moscow (21-23 May 2020)
- Regional conferences in Nizhny Novgorod (19-20 March 2020) and Belgorod (15-16 October 2020)
- pharmacology for bacteriologists and clinicians
- The first internet centre of distance education on antimicrobial chemotherapy in Russia
- prevention of infections caused by multi-resistant microorganisms".

Visit the website for more information.

APUA Nepal

update on sensitivity patterns of common isolates in urine and blood from hospitals of in Nepal. Read the newsletter here.

Antibiotic Resistance in the News

New strategy in the fight against antibiotic resistance

Bioscience engineers from KU Leuven in Belgium have developed a new antibacterial strategy that weakens bacteria by preventing them from cooperating. Unlike with antibiotics, there is no resistance to this strategy because the susceptible bacteria outnumber resistant ones. The findings are published in *Nature Communications*.

"Our aim is to introduce these new antimicrobials into clinical practice," explains Steenackers, co-author. "They can be used as a preventive medicine in the form of a pill, or as a coating on implants to reduce the risk of infections." The substance could also be used together with antibiotics.

Combining Multiple Antibiotics May Make Bacteria More Likely to Develop Resistance

Research published in <u>Science</u> shows that when patients are given a combination of antibiotics and develop tolerance to a single antibiotic in the combination, resistance to the second drug becomes more likely.

The authors monitored *Staphylococcus aureus* strains evolving in patients under treatment. They detected the rapid emergence of tolerance mutations, followed by the emergence of resistance, despite the combination treatment. This is the first study to demonstrate the process in people.

FDA launches app for healthcare professionals to report novel uses of existing medicines for difficult-to-treat infectious diseases

The US Food and Drug Administration (FDA) announced the global launch of <u>CURE ID</u>, an internet-based repository that will allow the clinical community to report their experiences with difficult-to-treat infectious diseases with novel uses of existing FDA-approved drugs through a website, a smartphone or other mobile device. The platform enables the crowdsourcing of medical information from healthcare providers to guide potentially life-saving interventions and facilitate the development of new drugs for neglected diseases.

Dual action anti-inflammatory and antibacterial gel treats wound infections

Researchers have developed a new antibacterial gel to treat wound infections that also has an immunosuppressive effect. The gel is based on the body's natural peptide defense for prevention of both bacterial infection and accompanying inflammation. The hydrogel was effective against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and clinical bacterial isolates *in vitro* and is a promising approach for wound healing. The study was published in *Science Translational Medicine*.

Association of the European Self-Care Industry (AESCI) releases position paper on AMR

The self-care industry is addressing the global threat of AMR by developing public health and health literacy campaigns at Member State level to educate European citizens on appropriate management of common winter illnesses and on infection prevention. These are often developed in partnership with public institutions and healthcare professionals. Read the paper in full.

Bacterial evolution of antibiotic weapons promises new insights for drug makers

Scientists at Trinity College Dublin have discovered how two chemically distinct species of bacteria naturally evolve antibiotic weaponry against their adversaries. By blueprinting precisely how the antibiotics function against methicillin-resistant *Staphylococcus aureus* (MRSA), the scientists have provided new options for drug designers.

These blueprints can now be used to guide pharmaceutical chemists when they design new, more effective drugs that are urgently needed in light of the accelerating global threat of antimicrobial resistance. Findings are published in Nature Communications.

Antibiotic prescription high in the absence of a documented indication in ambulatory care

A study in the <u>BMJ</u> identified a large number of ambulatory visits in which antibiotics were prescribed without a documented indication.

Antibiotic prescribing in the absence of a documented indication may severely bias national estimates of appropriate antibiotic use in this setting and misinform antimicrobial stewardship efforts. With 60% of antibiotic expenditure and up to 90% of antibiotic use originating in ambulatory care settings, more focus is needed to support well informed stewardship efforts beyond the hospital.

Smartphone could diagnose UTIs in 25 minutes

Researchers have developed a simple test to diagnose urinary tract infections (UTIs) that uses a smartphone camera. The system rapidly detects the presence of *E. coli* (present in 80% of UTIs) in urine samples.

It works by passing urine over a plastic strip containing the antibody that detects *E.coli*. An enzyme is added that changes colour which can be detected by a smartphone camera. Findings are published in *Biosensors and Bioelectronics*.

CDC: Core Elements of Hospital Antibiotic Stewardship Programs 2019



Hospital Leadership Commitment

Dedicate necessary human, financial, and information technology resources.



Accountability

Appoint a leader or co-leaders, such as a physician and pharmacist, responsible for program management and outcomes.



Pharmacy Expertise (previously "Drug Expertise"):

Appoint a pharmacist, ideally as the co-leader of the stewardship program, to help lead implementation efforts to improve antibiotic use.



Action

Implement interventions, such as prospective audit and feedback or preauthorization, to improve antibiotic use.



Tracking

Monitor antibiotic prescribing, impact of interventions, and other important outcomes, like *C. difficile* infections and resistance patterns.



Reporting

Regularly report information on antibiotic use and resistance to prescribers, pharmacists, nurses, and hospital leadership.



Education

Educate prescribers, pharmacists, nurses, and patients about adverse eactions from antibiotics, antibiotic resistance, and optimal prescribing

Japan had over 8,000 deaths related to drug-resistant bacteria in 2017

Researchers collected data on patients with bacteraemia caused by MRSA and fluoroquinolone-resistant *Salmonella*. MRSA deaths stood at 4,224 in 2017, although the number has been on the decline since 2011. *Salmonella* deaths were at 3,915, marking a continuous increase in the same period.

"As the number of MRSA deaths are falling, the government's measures against drug-resistant bacteria, including giving favourable treatments to hospitals promoting proper use of antibiotics, appear to be effective to a certain level," said Hiroshige Mikamo, an expert on the bacteria at Aichi Medical University.

But Mikamo called for reviewing the development of new drugs as well as how doctors choose drugs in treating patients, saying the annual number of deaths caused by the bacteria, including those not covered by the latest survey, is likely to "easily eclipse 10,000." <u>LINK</u>

Inappropriate Surgical Antimicrobial Prophylaxis Practices in Australia

A study in <u>JAMA Open Network</u> aimed to discern the current surgical antimicrobial prescribing practices in Australia and the factors associated with their appropriateness.

This quality improvement study of 9,351 surgical episodes found high rates of inappropriate procedural and postprocedural antimicrobial use across various hospital, patient and surgical factors.

The most common reason for inappropriate procedural use was incorrect timing, while duration greater than 24 hours was the most common reason for inappropriate postprocedural use.

These findings suggest that the identified hospital, patient, and surgical factors should be considered as targets for development of tailored interventions to ensure appropriateness of surgical antimicrobial prophylaxis prescriptions.

Vaccines vital to stopping antimicrobial resistance

A recent review of the progress made since publication of the Review on Antimicrobial Resistance (AMR Review) published in 2016 notes very little progress on the review's central recommendations. One of the recommendations was the development of new vaccines against disease in people and animals or a greater use of existing vaccines. The report highlights the challenges in demonstrating the magnitude that would convince policymakers that AMR is a reason to assign a much higher priority to vaccine use and development than they already do. For this reason, Wellcome has recently launched a research programme investigating the impact of vaccines on antibiotic use and / or AMR, with the aim of supporting and informing vaccine decision-makers around the world and tackling AMR. A WHO working group is aiming to create a roadmap that summarises priority actions for vaccine use and development by creating a value attribution framework that articulates the value of vaccines against AMR.

FDA approve new drug to treat UTIs

The FDA approved Fetroja (cefiderocol), an antibacterial drug for treatment of patients 18 years or older with complicated UTIs including kidney infections caused by susceptible Gram negative microorganisms, who have limited or no alternative treatment options.

The safety and effectiveness of Fetroja was demonstrated in a study of 448 patients with complicated UTIs. Of the patients who were administered Fetroja, 72.6% had resolution of symptoms and eradication of the bacteria approximately seven days after completing treatment, compared with 54.6% in patients who received an alternative antibiotic.

Labeling for Fetroja includes a warning regarding the higher all-cause mortality rate observed in Fetroja-treated patients compared to those treated with other antibiotics in a trial in critically ill patients with multidrug-resistant Gram-negative bacterial infections.

Antimicrobial consumption and resistance in *Escherichia coli* and *Klebsiella pneumoniae* European Union / European Economic Area

The trends of antimicrobial consumption of fluoroquinolones, third-generation cephalosporins and carbapenems and the AMR phenotypes reported in *Eurosurveillance* provide an indication that the recent public health efforts promoting prudent antimicrobial use are showing results. Nevertheless, percentages of AMR reported were comparatively much higher in 2018 than in 2002 / 06. Trends appear to stabilise or slow down rather than decrease in recent years. The results should encourage further efforts aiming to improve antimicrobial stewardship and infection prevention and control.

Under 5s in LMICs receive average 25 antibiotic prescriptions annually

A study in <u>The Lancet Infectious Diseases</u> assessed antibiotic exposure in children younger than 5 years in low— to middle—income countries (LMICs).

A cross-sectional study in sick children under 5 who attended a healthcare facility in an LMIC was performed between 2006 and 2016. 85.4% of healthcare facility visits were related to either a fever or cough. Antibiotics were prescribed to 80.5% of children diagnosed with respiratory illness; 50.1% with diarrhoea; and 28.3% with malaria. The mean number of antibiotic prescriptions issued to children between birth and age 5 years across the eight LMICs was 24.5, ranging from 7.1 in Senegal to 59.1 in Uganda.

Antibiotic stewardship should focus on reducing and optimising antibiotic use in patients with COPD

Patients with chronic obstructive pulmonary disease (COPD) receive three times more antibiotic prescriptions in primary care than the general population. Researchers used electronic health records from primary care to identify which types of COPD patients get the most antibiotics to inform on appropriate antibiotic stewardship.

The study, published in <u>Journal of Antimicrobial Chemotherapy</u>, included 157 practices with a total of 19,594 patients diagnosed with COPD. Researchers found that patients with severe COPD accounted for 13% of antibiotics prescribed and those with mild—severe COPD received 42.5% of all prescriptions. Targeting patients with moderate to low COPD would be the most effective way to reduce antibiotic use.

Publications / Resources of Interest

Superbugs podcast series. Queensland University.

Antimicrobial Stewardship programmes in health-care facilities in low- and middle- income countries: A WHO practical toolkit. World Health Organisation

Superbugs Unplugged. Podcast initiative by U.S. PIRG and the Antibiotic Resistance Action Center

<u>Survey of healthcare workers' knowledge, attitudes and behaviours on antibiotics, antibiotic use and antibiotic</u> resistance in the EU/EEA. European Centre for Disease Prevention and Control.

Scottish One Health Antimicrobial Use and Antimicrobial Resistance in 2018. Health Protection Scotland

English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR). Public Health England.

Antimicrobials Sold or Distributed for Use in Food-Producing Animal. The U. S Food and Drug Administration

Webinar: Launch of the curricula guide for health workers' education and training on AMR. WHO / Public Health England.

PHE infectious diseases strategy 2020 —2025. Public Health England.

Ardal C et al. <u>Antibiotic development — economic, regulatory and societal challenges</u>. *Nat Rev Microbiol*. 2019;136:105458

Zhang, M et al. <u>Variation of antibiotic resistome during commercial livestock manure composting</u>. *Environ Int*. 2020;8:136:105458

Manoli K et al. <u>Inactivation of Murine Norovirus and Fecal Coliforms by Ferrate(VI) in Secondary Effluent</u> Wastewater. *Environ Sci Technol*. 2020 Jan 13

Van Gompel *et al*. The antimicrobial resistome in relation to antimicrobial use and biosecurity in pig farming, a metagenome-wide association study in nine European countries. *J Antimicrob Chemother*. 2019;74:865-876

Events



Antimicrobials 2020: 21st Annual Meeting of Australian Society for Antimicrobials

27-29 February 2020

Melbourne Convention and Exhibition Centre, Melbourne, Australia

21st Annual Scientific Meeting



Annual Congress of the Lebanese Society of Infectious Diseases and Clinical Microbiology

27-29 February 2020

Le Royal Hotel, Beirut, Lebanon



BSAC Spring Conference 2020

16-17 March 2020

Queen Elizabeth Conference Centre, Westminster, London



<u>Decennial International Conference on Healthcare-Associated Infections</u>

Atlanta, GA 26 -30 March 2020

Global Solutions to Antibiotic Resistance in Healthcare



International Symposium on Staphylococci and Staphylococcal Infections (ISSSI) 2020

23 -26 August 2020 Perth, Australia



32nd International Congress of Antimicrobial Chemotherapy

Co-hosted by Australian Society for Antimicrobials

21—24 November 2021

Perth Convention Centre, Australia

About APUA

Founded in 1981 by Prof. Stuart B. Levy as a global non-profit organisation, APUA's mission is to maximise the effectiveness of antimicrobial treatment by promoting appropriate antimicrobial use and containing drug resistance. It was the first organisation to address antibiotic preservation and continues to provide a strong voice in the field despite the subsequent emergence of many other organisations and groups addressing a topic which has become a specialty in its own right; that of "antibiotic stewardship".

APUA has affiliated Chapters in 19 countries. The APUA network facilitates the exchange of objective, up-to-date scientific and clinical information among scientists, health care providers, consumers and policy makers worldwide.

Prof. Levy's retirement was announce towards the end of 2018. This was an opportunity for the APUA Board to review its leadership and governance and it took the opportunity to seek a partner organisation with which to synergise. This led to the merger of APUA with the International Society of Antimicrobial Chemotherapy (ISAC), effective from February 2019.

About ISAC

ISAC was founded as a non-profit organisation in 1961 and, in response to the dynamic nature of the subject matter, has focused most recently on antimicrobial stewardship and antimicrobial resistance.

ISAC is a federation of affiliated Member Societies which aims to increase the knowledge of antimicrobial chemotherapy and combat antibiotic resistance around the world.

ISAC currently has a worldwide membership of 88 national and regional societies, which in turn have over 50,000 individual members.

ISAC has two society journals:

- International Journal of Antimicrobial Agents (IJAA)
- Journal of Global Antimicrobial Resistance (JGAR)

ISAC's scientific congress, International Congress of Antimicrobial Chemotherapy (ICC), is held every two year and it is now in its 32nd year.

For more information on ISAC, visit www. ISAC.world

