Antimicrobial stewardship programs

In resource poor settings

Prof. Gunturu Revathi
Dept. of Pathology
The Aga Khan University Hospital
Nairobi
ICAN Harare, Zimbabwe
A 35-year-old female
no past medical history presents to the A&E
complaining of
cough and shortness of breath for 2 days that is
progressively worsening.

On physical examination,

She is febrile with an oxygen saturation of 94% on
room air

Decreased breath sounds at the right base.

A chest x-ray shows right lower lobe consolidation.
70-year-old female with fever, nausea, and back pain for 3 days.

Her daughter states her mother had a similar presentation when she had a UTI 2 years ago.

She is febrile to 38.3°C (101°F), with left costo-vertebral angle tenderness.

Her urine dipstick is positive for leukocyte esterase and nitrites.
An 85-year-old male brought in for evaluation for fever. He has a history of insulin-dependent diabetes mellitus, hypertension, and dementia.

On physical examination, he is febrile, with otherwise normal vital signs.

His abdomen is slightly distended, soft, but diffusely tender to palpation.
Is this disease.....

really the same as this disease?
Evidence-Based Guidelines For Evaluation And Antimicrobial Therapy For Common Emergency Department Infections
The antimicrobial agents – unique drugs.

Efficacy is higher than others in reduction of morbidity and mortality.

Antibiotics are the only group of drugs with ecological effects, contribute to the emergence and spread of microbial resistance.

Finally, they are used by almost all medical specialties.

Appropriate use of antimicrobials is highly complex because of the important advances in the management of infectious diseases and the wide spread of antibiotic resistance.
The remarkable success of antibacterial agents

Infectious Disease Mortality Rate per 100,000 inhabitants

“Drug resistance follows the drug like a faithful shadow.”

- Paul Erhlich 1854-1915
A Matter of Life and Death
The Economics of Antibiotic Resistance

BY RAMANAN LAXMINARAYAN

Third Quarter 2012
ANTIBIOTIC RESISTANCE THREATS
in the United States, 2013
COMBAT DRUG RESISTANCE

No action today, no cure tomorrow

World Health Organization

World Health Day 2011
The evolving threat of antimicrobial resistance
Options for action
Patients for Patient Safety

Patients as Partners

Les patients en tant que partenaires

El paciente como aliado

与病人并肩合作

El paciente como aliado

El paciente como aliado

المرضى كشركاء

World Health Organization

Patient Safety

A World Alliance for Safer Health Care
Carbapenem and 3rd. gen. cephalosporin resistance among *K. pneumoniae* is increasing in all patient settings

Note: Data for 2010 available through July.

Mechanisms of Resistance

Enzymatic inhibition

Decreased uptake

Increased export

Altered target

Metabolic bypass
The Antibacterial Drug Pipeline is virtually empty
Factors contributing to increased resistance

- Overuse of antimicrobials
- Use of broad spectrum agents
- Low dosages
- Improper frequency
- Extended duration of therapy
- Prophylactic use
Situations where antimicrobials are used excessively

- Acute Upper respiratory tract infections.
- Acute gastroenteritis.
- Acute urinary tract infection.
- Surgical prophylaxis.
- Pyrexia of unknown origin.
- Undiagnosed fever in the immune-suppressed.
Community-Acquired Pneumonia: Atypical Pathogens

Worldwide Incidence of Atypical Pathogens
University of Louisville Infectious Diseases Atypical Pathogens Reference Laboratory Database

Region I: 22% North America
Region II: 28% Europe
Region III: 21% Latin America
Region IV: 20% Asia and Africa

Pressures on the primary care physician

Peer groups / prescribing and pharmacy advisors

Pharmaceutical representatives
(Industry spends 35% of profits on marketing)

Regulatory control mechanisms

Patients’ demands and physician aspirations

Hospital experts, formularies and guidelines
Why don’t physicians follow guidelines?

RTI guidelines… lowest grades of evidence

- Barriers to implementation include lack of:
  - Awareness / familiarity
  - Agreement: between guidelines and ‘experts’
  - Time and motivation
  - Credibility (applicability and practicability)
  - Proven outcome benefit

- TOO MUCH INPUT
- MANY CONFLICTS
- I AM TOO BUSY
- WHICH ‘EXPERTS’
- BENEFIT TO ME
- PROVE IT!

*Cabana et al. JAMA* 1999; 282:1458
Mammography: Study Finds No Lives Saved
Published: Feb 11, 2014 | Updated: Feb 13, 2014

Annual mammography failed to reduce breast cancer mortality in women, ages 40 to 59, compared with physical examination or routine care, based on 25–year follow-up data from a Canadian screening program.

NIH to Researchers: Credibility Counts
Published: Jan 27, 2014 | Updated: Jan 27, 2014

One report - "as many as two-thirds of studies related to preclinical animal trials were not able to be reproduced problem is not scientific fraud but a combination of factors -- including the pressure to publish rapidly and poor training in experimental design
Why Most Published Research Findings Are False


Published online Aug 30, 2005.

John P. A. Ioannidis

Stanford University School of Medicine in Stanford, Calif.
Evidence-based medicine (EBM) is the new *mantra*.

The best available evidence be used to aid clinical decision-making and policy.

**EBM has changed medical practice.**

It raises many questions.

**Randomized controlled trials (RCT) – the cornerstone of EBM.**

Extrapolating knowledge from RCTs to individual patients across different settings – a big problematic.

Such extrapolations require much more evidence, which is often unavailable.
Evidence is needed for

Efficacy ("Can it work?")

Effectiveness ("Does it work in practice?")

Efficiency ("Is it worth it?")

All of these need to be considered.
Most trials test for efficacy in ideal situations using

- Detailed protocols,
- Carefully selected patients
- Placebo controls,
- Good treatment compliance
- And intensive follow-up.
These ideals – rarely achievable in routine clinical practice with

Poor diagnostic accuracy,

Poor patient compliance

And partial patient coverage
Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials.
The problem: mismatch between antibiotic usage and need

Antibiotic Usage

Actual need for antibiotics

The solution: 1) reduce antibiotic usage 2) align reduced usage with actual need
Tragic Paradox in Developing countries
Kenya is no exception
The World Health Organization (WHO) estimates — < 25% of children with pneumonias receive antibiotics, resulting in significant mortality.

Mortality in adults with bacterial infections — a major concern.

Lack of access to affordable medical care for the vast majority of the rural population

The urban-centric nature of our health care delivery system contributes to preventable deaths
The current scenario in developing countries makes antibiotic stewardship quite challenging.

Absence of lab services of any kind.

Diagnosis of serious infective conditions including acute meningitis, childhood TB, is made based on clinical algorithms.

Majority of the public health care facilities operate without a clinical laboratory.
A lot of empirical prescribing in private clinics
In public sector by clinical officers with limited training and scanty updating of medical knowledge
Lab facilities not available / not accessible / too expensive
Major areas of concern

- Lack of emphasis on specific diagnosis / Clinical misdiagnosis,
- Inadequate health care infrastructure
- Laboratory capability and diagnostic accuracy
Lack of emphasis on lab diagnosis of infectious diseases – clinician apathy and a culture of syndromic approach

Concept that microbiology is expensive and time consuming

Perceptions that Lab results can not be trusted – Justified indeed!
I AM CONCERNED ABOUT THE HIGH LEVELS OF BLOOD WE FOUND IN YOUR BLOOD TEST
HEAVY MIXED GROWTH OF THREE TYPES OF COLONIES
Why is there an “increase” in the diagnosis of Enteric Fever (Typhoid)?

- Motivated by money-making ideas e.g. to sell the Widal Test kits
- Increased unprofessionalism
- Presence of many fake laboratories & quacks
- Presence of fake reagents
- Lack of supervision/prosecution
Microbiology depts. in medical colleges staffed by veterinary graduates for lack of other qualified personnel.

Pathology trainees tend to spend the least possible time in microbiology section.

Infectious disease consults are hardly ever available even in major hospitals.
Knowledge Gaps

- Almost nothing known about antibiotic resistance in the community
- What drives antibiotic prescribing? UNKNOWN!
- Antibiotic treatment guidelines: how are they used and how effective they in patient treatment? UNKNOWN!
- Staff in many hospitals lack access to guidelines, even if they know about their existence
Total absence of any kind of surveillance system for general antibiograms.

The ongoing HIV pandemic opportunistic infections populations on septrin and fluconazole prophylaxis.
A vicious cycle exists between adequate facilities and competent personnel -

LOW MORALE

A WHO external QA survey revealed - Few labs supervised by pathologists / qualified microbiologists

Any small number of microbiologists lost to Brain drain or Brain in the drain
Barriers effective laboratory services in resource poor countries including sub-Saharan Africa

- Laboratory infrastructure Problems
- Lack of laboratory consumables
- Essential equipment
- Skilled personnel
- Educators and training programs
- Insufficient monitoring of test quality
- Absence of governmental standards for laboratory testing
Potential solutions could be –

- Emphasize importance of laboratory testing,
- Allocation of financial resources,
- Strengthen the existing health care infrastructure,
- Monitor test quality,
- System for laboratory accreditation,
- Laboratory training programs,
- Partnerships between public and private organizations
- Introduction of affordable, rapid diagnostic tests.
Fifty-eighth session
Yaounde, Republic of Cameroon, 1–5 September 2008

Provisional agenda item 7.4

STRENGTHENING PUBLIC HEALTH LABORATORIES IN THE WHO AFRICAN REGION: A CRITICAL NEED FOR DISEASE CONTROL

Report of the Regional Director
• Considerable challenges for microbiology laboratory services in the Africa Region.

• Need for a combination of complementary measures, strategies and capacity strengthening

• Developing a comprehensive national laboratory policy to address the key issues.
RESOLUTION

STRENGTHENING PUBLIC HEALTH LABORATORIES IN THE WHO AFRICAN REGION: A CRITICAL NEED FOR DISEASE CONTROL (document AFR/RC58/6)

The Regional Committee,

Aware of the crucial role that laboratories play in disease prevention, control, alert and response to epidemics and health research;

Acknowledging the important role of laboratories in Integrated Disease Surveillance and implementation of the International Health Regulations;

Concerned about the frequent occurrence of outbreaks in the Region that are not immediately detected and responded to due to inadequate laboratory capacities;

Recognizing the weak organizational, financial and human resource capacity and low investment in laboratory services;

Concerned about the unclear oversight arrangement and the role of laboratory services within the national health systems in some Member States;

Cognizant of the need for Member States to ensure availability of quality laboratory services;

Acknowledging the need for national laboratory policies to guide the development and proper functioning of national laboratory networks in Member States;

1. ENDORSES the report of the Regional Director on strengthening public health laboratories in the WHO African Region;
Lab Cap Africa program countries

Botswana, Côte d'Ivoire, Ethiopia, Kenya, Mozambique, Namibia, Nigeria, Rwanda, Tanzania, Zambia
Welcome to East Africa Public Health Lab Network Bulletin, a quarterly newsletter from the Department of Disease Prevention and Control, Ministry of Public Health and Sanitation. Being the first one of its kind, its believed that it will give health workers in particular laboratory professionals the forum discuss issues of current and new diagnostic services, disease surveillance, training programs and operational research on TB and other communicable diseases such as Cholera, meningitis, influenza, polio and Drug Resistant TB that are of public health concern. Future issues will include discussions and interaction between health care workers and members of the public on issues pertaining to laboratory diagnosis and how the laboratory assists in the betterment of health in both public and private sectors in Kenya and the East Africa region. We encourage comments and remarks from readers, workers et al. in shaping the pattern of the future releases.

Let us together strive for an infection free community.

[Signature]
Laboratory Information System (LIS)

The idea of implementing LIS in Kenya was developed in 2007. The National Public Health Laboratory Services (NPHLS) engaged the Centers of Disease Control and Prevention (CDC)-Kenya to support implementation of suitable software for LIS. The CDC-funded Association of Public Health Laboratories (APHL) was chosen as the partner to support this implementation which was to be done in phases. The priority sites in the first phase of implementation were the three central reference laboratories (HIV, TB and Microbiology).

Successes
Three central reference laboratories are fully utilizing the LIS system (Nairobi, Coast, R.Valley). Turnaround time has substantially been reduced. Sample management has been streamlined and workflow harmonized. Since each laboratory has its own sample tracking and work flow process so far, electronic LIS is the way to go. This vision is based on the following:-

1. Accreditation
As laboratories move to attain the WHO accreditation status, there is need to establish an efficient sample tracking and work flow process mechanisms of streamlining work flow processes to cope with this demand.

2. Operational research
Apart from diagnostic and public health function of medical laboratories, operational research is gaining momentum given the
Antimicrobial stewardship + Infection control program

Can limit the emergence and transmission of antimicrobial-resistant bacteria
Antimicrobial stewardship refers to the multifaceted approach (including policies, guidelines, surveillance, prevalence reports, education and audit of practice) that healthcare organizations have adopted to optimize prescribing.
Aims of Antimicrobial Stewardship

- The aim of AMS programs is to improve its use in the context of every clinical situation, according to characteristics of every patient.
- This implies the correct drug selection, with an adequate/balanced spectra – avoiding higher spectra in the majority of situations- and with a correct/rational moment, dose, route of administration and treatment duration.

Two core members:

- An infectious diseases physician
- A clinical pharmacist with infectious diseases training.

- Other critical members of the team can include a clinical microbiologist, a hospital epidemiologist, an infection control professional, and an information system specialist.
Efficacy of Antimicrobial Stewardship Programmes: Cochrane Review.

- 77% showed one significant improvement in at least one outcome.
- 57 interventions looked for reduction in ATB consumption.

Material and technical resources

- stable drug supply;
- microbiology laboratory diagnosis tools;
- basic supplies for an effective IPC programme;
- computer support, intranet and internet connection;
- updated data on bacterial resistance and antimicrobial consumption;
- pharmacokinetic/pharmacodynamic dose optimisation
ANTIBIOTIC STEWARDSHIP
IN YOUR FACILITY WILL

DECREASE
- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE
- GOOD PATIENT OUTCOMES

PROMOTE ANTIBIOTIC BEST PRACTICES—
A FIRST STEP IN ANTIBIOTIC STEWARDSHIP

- ENSURE ALL ORDERS HAVE DOSE, DURATION, AND INDICATIONS
- GET CULTURES BEFORE STARTING ANTIBIOTICS
- TAKE AN “ANTIBIOTIC TIMEOUT” REASSESSING ANTIBIOTICS
  AFTER 48-72 HOURS

ANTIBIOTIC STEWARDSHIP PROGRAMS ARE
A “WIN-WIN” FOR ALL INVOLVED

A UNIVERSITY OF MARYLAND STUDY SHOWED
ONE ANTIBIOTIC STEWARDSHIP PROGRAM
SAVED A TOTAL OF $17 MILLION
OVER EIGHT YEARS

ANTIBIOTIC STEWARDSHIP HELPS IMPROVE
PATIENT CARE AND SHORTEN
HOSPITAL STAYS, THUS BENEFITING
PATIENTS AS WELL AS HOSPITALS
A pre-prescription or ‘front-end’ strategy

restricted availability of certain drugs
pre-authorisation of some antimicrobials

A post-prescription or ‘back-end’ approach

a prospective audit and feedback
Both front-end and back-end strategies are beneficial.

Most successful ASPs usually combine them.
INFECTION CONTROL

Surveillance
(Outcome & Process)

Isolation of patient & Use of Personal Protective Equipment
Hand Hygiene
Antibiotic Policy
Aseptic technique, sterile equipment
Environment
Cleaning, waste disposal etc

from: Damani N N, 2003
Figure 43-2 Organizational structure of a comprehensive antimicrobial management program. (Adapted from John JF Jr, Fishman NO. Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospitals. Clin Infect Dis. 1997;24:471.)
Antimicrobial Stewardship
Prudent use of antibiotics +
Infection control

- Inhibition of non-pathogenic bacteria
- Selection of resistant mutants
- Toxicity / side effects
APPENDIX D: SURGICAL PROPHYLAXIS

The generally accepted principles of antimicrobial prophylaxis in surgery involve five considerations.
<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>67%</td>
</tr>
<tr>
<td>Europe</td>
<td>65%</td>
</tr>
<tr>
<td>Asia</td>
<td>53%</td>
</tr>
<tr>
<td>Oceania</td>
<td>48%</td>
</tr>
<tr>
<td>South America</td>
<td>46%</td>
</tr>
<tr>
<td>Africa</td>
<td>13%</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>FHKV, n = 459</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------</td>
</tr>
<tr>
<td></td>
<td>ICU</td>
</tr>
<tr>
<td>Amikacin</td>
<td>74.2</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>6.9</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>0</td>
</tr>
<tr>
<td>Cefepime</td>
<td>20.2</td>
</tr>
<tr>
<td>Cefaperazone</td>
<td>20</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>28.9</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>21.2</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>22.5</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>12.4</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>38.2</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>51.7</td>
</tr>
<tr>
<td>Imipenem</td>
<td>100</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>12.8</td>
</tr>
<tr>
<td>Meropenem</td>
<td>100</td>
</tr>
<tr>
<td>Neflumycin</td>
<td>67.4</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>83.0</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>10.6</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>4.7</td>
</tr>
<tr>
<td>Piperacillin + Tazobactum</td>
<td>53.9</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>31.3</td>
</tr>
</tbody>
</table>
BacLink software
Import & analyze antimicrobial susceptibility data from software / automated ABST instruments
“It checks out OK on the computer… now let's confirm it with the pendulum”
Current status of Antimicrobial Resistance among clinical Bacterial isolates in city hospitals.

Periodically circulated by various private hospitals

But

95% of infections are treated in out-patient settings.

No information available on them.
Microbiology Spectrum and Susceptibility
## Antimicrobial Susceptibilities, 2012-2013

**Urine cultures in outpatients, main lab AKUHN (% susceptible)**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number</th>
<th>Amp</th>
<th>Amox/Clav</th>
<th>Amikacin</th>
<th>Cipro</th>
<th>Cefotax</th>
<th>Cefurox</th>
<th>Ntfn</th>
<th>Gent</th>
<th>Merop</th>
<th>TMP/SMX</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli 2012</td>
<td>1122</td>
<td>20%</td>
<td>67%</td>
<td>100%</td>
<td>66%</td>
<td>81%</td>
<td>77%</td>
<td>87%</td>
<td>84%</td>
<td>100%</td>
<td>24%</td>
</tr>
<tr>
<td>E. coli 2013</td>
<td>1025</td>
<td>21%</td>
<td>68%</td>
<td>100%</td>
<td>65%</td>
<td>78%</td>
<td>75%</td>
<td>86%</td>
<td>83%</td>
<td>100%</td>
<td>26%</td>
</tr>
<tr>
<td>E coli total</td>
<td>2147</td>
<td>21%</td>
<td>67%</td>
<td>100%</td>
<td>66%</td>
<td>79%</td>
<td>76%</td>
<td>86%</td>
<td>84%</td>
<td>100%</td>
<td>25%</td>
</tr>
<tr>
<td>K peumo 2012</td>
<td>142</td>
<td></td>
<td>56%</td>
<td>99%</td>
<td>85%</td>
<td>72%</td>
<td>70%</td>
<td>N/A</td>
<td>80%</td>
<td>99%</td>
<td>39%</td>
</tr>
<tr>
<td>K. pneumo 2013</td>
<td>140</td>
<td></td>
<td>49%</td>
<td>99%</td>
<td>74%</td>
<td>59%</td>
<td>56%</td>
<td></td>
<td>67%</td>
<td>99%</td>
<td>42%</td>
</tr>
<tr>
<td>K pneumo total</td>
<td>282</td>
<td></td>
<td>53%</td>
<td>99%</td>
<td>79%</td>
<td>66%</td>
<td>63%</td>
<td>73%</td>
<td>99%</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td>Proteus total</td>
<td>61</td>
<td>89%</td>
<td>100%</td>
<td>93%</td>
<td>98%</td>
<td>97%</td>
<td></td>
<td>90%</td>
<td>100%</td>
<td>30%</td>
<td></td>
</tr>
</tbody>
</table>
The face of Self medication Should be discouraged by all means

Questions – in a poor country –
Public health facilities hardly able to help
Private care is too expensive
How is a person to keep himself alive?
Self medication is a desperate attempt most of the time.
I'VE ALREADY GOT A DIAGNOSIS FROM HOMEFLC.COM... BUT I THOUGHT I'D SEE YOU FOR A SECOND OPINION!
Use of antimicrobials in Animal husbandry, Poultry and Agriculture

A major factor Creating and Disseminating resistant bacteria in the environment.

Our food is heavily contaminated with antibiotics.
The Doctor’s Dilemma

No response to intense antibiotic therapy!!!
Lets see if there is any response to intense litigation.

Choose between patient welfare and directives of the healthcare system may be penalties or incentives.
Summary

• Antimicrobial resistance has reached dangerous levels.
• Prescribing practices have to change.
• Adherence to the principles of Evidence Based Practice is essential.
• AMR Surveillance is crucial.
• Diagnostics have to improve
• Control of antibiotics imperative in human & animal use.
• Intense need to discover new antimicrobials & vaccines and new rapid, reliable and cost effective diagnostics for infectious diseases.
Thank You