Learning Objectives of the Lecture

I hope, by the end of this lecture you will be able to:

• Recognize the growing problem of antibiotic resistance.

• Identify current antibiotic resistance trends in select microorganisms.

• Describe various antimicrobial stewardship intervention strategies.
Outline of the lecture

• Background: discovery, sources, uses, classes and mechanism of action of antibiotics.

• Antibiotic resistance:
  – Emergence of antibiotic resistance,
  – Antibiotic resistance in the Middle East and North Africa (MENA) region.

• Efforts to combat antibiotic resistance:
  – Global initiatives to address antibiotic resistance.
  – The role of antimicrobial stewardship programs.

• Antibiotic discovery.
Paul Ehrlich’s magic bullets

- **Methylene blue** to fight malaria (1891), **trypan red** against trypanosomes (1904).
- Later in 1910, **Ehrlich’s** and **Saha-chiro Hata**, discovered “**compound 606 or Salvarsan**”, which was used to treat syphilis.
- Ehrlich’s coined the term **“magic bullet”**, to define compounds effective against microbes thus, paving the way for antibiotic discovery.
Alexander Fleming and penicillin

- 1928, penicillin: *Penicillium notatum* (*Penicillium chrysogenum*).
- Clinical use of penicillin - early 1940s.
- Since then over 3,000 compounds with antibiotic properties have been discovered.
- However, only 135 antibiotics are in clinical use today.

https://www.google.com/search?q=alexander+fleming&source=lnms&tbm
Antibiotics

- **Antibiotic**: is a chemical (drug) that kills or inhibits the growth of bacterial microorganisms.

Antibiotics can be classified:

- by **activity** as: bactericidal or bacteriostatic.
- by **target specificity**: narrow-spectrum vs broad-spectrum.
- by **mechanism of action**:
  - Cell wall synthesis inhibitors,
  - Protein synthesis inhibitors,
  - Nucleic acids (DNA and RNA) synthesis inhibitors,
  - Mycolic acid synthesis inhibitors,
  - Folate metabolism inhibitors,
  - Cytoplasmic membrane inhibitors.
- by **classes**: based on the chemical structure, there are about 17 classes.
Antibiotics: mechanism of action

**Cell wall synthesis**
- Cycloserine
- Vancomycin
- Bacitracin
- Penicillins
- Cephalosporins
- Monobactams
- Carbapenems

**DNA gyrase**
- Nalidixic acid
- Ciprofloxacin
- Novobiocin

**RNA elongation**
- Actinomycin

**DNA-directed RNA polymerase**
- Rifampin
- Streptovaricins

**Protein synthesis (50S inhibitors)**
- Erythromycin (macrolides)
- Chloramphenicol
- Clindamycin
- Lincomycin

**Folic acid metabolism**
- Trimethoprim
- Sulfonamides

**Protein synthesis (30S inhibitors)**
- Tetracyclines
- Spectinomycin
- Streptomycin
- Gentamicin
- Kanamycin
- Amikacin
- Nitrofurans

**Cytoplasmic membrane structure**
- Polymyxins
- Daptomycin

**Cytoplasmic membrane**
- PABA

**Cell wall**
- Ribosomes

**Figure 20-14 Brock Biology of Microorganisms 11/e © 2006 Pearson Prentice Hall, Inc.**
Antibiotics: grouping by classes

**B-LACTAMS**
- Commonly used as bacteriostatic agents, restricting growth & reproduction
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**AMINOGYCOSIDES**
- Family of over 20 antibiotics
- **Key:** Commonly used as bactericidal agents, causing bacterial cell death

**CHLORAMPHENICOL**
- Commonly used in low income countries
- **Key:** Commonly act as bactericidal agents, causing bacterial cell death

**GLYCOPEPETIDES**
- Consist of carbohydrate linked to a peptide formed of amino acids
- **Key:** Commonly act as bactericidal agents, causing bacterial cell death

**QUINOLONES**
- Resistance evolves rapidly
- **Key:** Commonly act as bactericidal agents, causing bacterial cell death

**OXAZOLIDINONES**
- Potent antibiotics commonly used as "drugs of last resort"
- **Key:** Commonly act as bactericidal agents, causing bacterial cell death

**DISCOVERY**
- 1930
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**SULFONAMIDES**
- First commercial antibiotics were sulfonamides
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**TETRACYCLINES**
- Becoming less popular due to development of resistance
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**MACROLIDES**
- Second most prescribed antibiotics in the NHS
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**ANSAMYCINS**
- Can also demonstrate antiviral activity
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**STREPTOGRAMINS**
- Two groups of antibiotics that act synergistically
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**LIPOPEPTIDES**
- Instances of resistance rare
- **Key:** Commonly act as bacteriostatic agents, restricting growth & reproduction

**EX Closures**
- Antibiotics in the Nhs, such as amoxicillin and flucloxacillin; Cephalosporins such as cefalexin.
- Distinct individual compound
- All contain fused aromatic rings with a carboxylic acid group attached
- All contain 2-oxazolidinone somewhere in their structure
- All contain a beta-lactam ring
- All contain aminosugar substructures
- All contain a beta-lactam ring
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Source: http://www.compoundchem.com/2014/09/08/antibiotics/
Antibiotics: sources and uses

Three major sources:

- **Fungi**: *Penicillium*, *Cephalosporium*
- **Bacteria**: *Actinomycetes*, *Bacillus spp*
- **Lab**: synthetic or semisynthetic

Why do we use antibiotics?

- To treat Infections.
- To prevent Infections (prophylaxis).
- To promote growth (livestock and fish farming).
The “miracle” of antibiotic

- Discovery of penicillin revolutionized treatment of infectious diseases.
- Antibiotics decreased morbidity/mortality rates, and increased life expectancy due to ability to prevent and treat infections.

Armstrong GL et al, JAMA 1999; 281(1) 61-66
Antibiotics continue to save lives everyday.

- The ability to control infections in clinical practice (such as those listed below), have been possible largely due to the availability of effective antibiotics to prevent and manage infections.
  - Neonatal care
  - Transplantation
  - Chemotherapy
  - Immunosuppression
  - Complex and routine surgery
  - Obstetric care
  - Intensive care interventions
But...antibiotics are a limited resource

Increasing antibiotic resistance.

Increased inappropriate use of antibiotics.

Decreasing pipeline of new antibiotics.

Urgent call to action

The ongoing explosion of antibiotic-resistant infections continues to plague global and US health care. Meanwhile, an equally alarming decline has occurred in the research and development of new antibiotics to deal with the threat. In response to this microbial "perfect storm," in 2001, the federal Interagency Task Force on Antimicrobial Resistance released the "Action Plan to Combat Antimicrobial Resistance; Part 1: Domestic" to strengthen the response in the United States. The Infectious Diseases Society of America (IDSA) followed

Antibiotic resistance is an emerging threat to public health: an urgent call to action at the Antimicrobial Resistance Summit 2011

A national interdisciplinary body is urgently needed to manage the looming antimicrobial resistance crisis

The introduction of antibiotics was one of the most important developments in modern medicine. Their availability has facilitated increasingly complex care and, not surprisingly, microbial resistance to antibiotics has been identified as one of the greatest threats to human health. A return to the "pre-antibiotic era" would render many routine infections untreatable and would seriously affect current practice in surgery, intensive care, organ transplantation, neonatology and cancer services through major increases in morbidity and mortality. The time to act is now — before we lose these "miracle" drugs for good.
Emergence of antibiotic resistance

“ It is not difficult to make microbes resistance to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body.”

….. The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under-dose himself, and by exposing his microbes to non-lethal quantities of the drug make them resistant”

Sir Alexander Fleming’s Nobel Lecture, Dec 11th, 1945
Antibiotic Resistance

Pssst! Hey kid! Wanna be a Superbug...?
Stick some of this into your genome...
Even penicillin won't be able to harm you...

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.
Antimicrobial Resistance (AMR)

- **Antimicrobial resistance (AMR):** is the ability of a microorganism (bacterium, fungus, virus, parasite) to stop an antimicrobial agent (antibiotic, antifungal, antiviral, antiparasitic) from working against it.

- **Antibiotic Resistance:** a condition in which there is a bacterial insensitivity to an antibiotic that usually causes growth inhibition or cell death at a given concentration.

Source: http://3glol.net/2014/01/22/antibiotic-resistance-r-u-n-danger/
The time between discovery of a new antibiotic and development of resistance has become much shorter over the last 40 years.
Development of antibiotic resistance in *Staphylococcus aureus*: a rapid journey

Year of Antibiotic Release

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<tr>
<th>Year of Antibiotic Release</th>
<th>Chloramphenicol</th>
<th>Tetracyclines</th>
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Year of Reported Resistance

Year of first use and then clinical resistance for each antibiotic

Antibiotic resistance: causes

- Inappropriate use (misuse, overuse, etc.. see next slide).

http://www.who.int/mediacentre/events/2015/infographics/en/
Antibiotic use and antibiotic resistance

- Relationship between total antibiotic consumption and *Streptococcus pneumoniae* resistance to penicillin in 20 industrialised countries.

Source: http://www.who.int/patientsafety/implementation/amr/publication/en/
Antibiotic resistance: causes

- Inappropriate use (misuse, overuse, etc.).
- Inadequate diagnostics.
- Poor infection control in hospitals.
- Antibiotic use in animal husbandry and food.
- Globalization and travel.
- Substandard & falsified antibiotics.
- Natural (biological) causes, such as mutations and gene transfer.

http://www.who.int/mediacentre/events/2015/infographics/en/
Mechanism of antibiotic resistance

- **Intrinsic resistance** via: a) **blocked penetration**: a variety of Gram-negative bacteria reduce the uptake of certain antibiotics, such as beta lactams, by modifying the cell membrane *porin* channel frequency, size, and selectivity.

- b) **Efflux pump**: some bacterial membrane proteins act as an efflux pump extruding antibiotics out of the cell, e.g., *E. coli* for tetracycline.

- **Adaptive resistance**: arises due to active alterations in the genetic make-up, and/or protein expression such as antibiotic *target site modification*.

- **Acquired resistance**: results from acquisition of antibiotic resistance genes via plasmids, integrons, transposons, etc... from an antibiotic resistant microbe, e.g., beta lactamases.

Source: https://courses.lumenlearning.com/microbiology/chapter/drug-resistance/
Antibiotic Resistance in MENA Region

Source: https://www.ryah.ca/2014/09/29/animal-health-week-antibiotic-responsible-and-appropriate-use/
MENA Methicillin resistant *S. aureus* (MRSA) rates among *S. aureus* isolates.

**Source:**
1: Sudan: http://apps.who.int/medicinedocs/en/d/Js22201en/
2: Iran: Rahimi et al., 2014
3: Jordan, Lebanon, Tokajian et al., 2014
4: Qatar: El-Mahdy et al., 2014
5: Libya: Buzaid et al., 2011
6: Iraq: Edgie-Mark et al., 2011
7: Saudi Arabia: El Amin et al., 2012
8: Kuwait: Boswihi, S., et al., 2016
9: Algeria: Antri et al., 2010
10: Egypt: Khairalla et al., 2017
Steady increase in MRSA prevalence in Qatar

Source: Dr. Emad Ibrahim, HMC Microbiology and Virology Division, 2017, unpublished data.
Alarming levels of multidrug-resistant tuberculosis (MDR-TB)

**Tuberculosis worldwide**

An estimated 2-3 billion people are infected with the bacillus *Mycobacterium tuberculosis*, only 5-15% will develop the disease.

*In 2015*
- 10.4 million cases
- 1.8 million deaths
- 480,000 *MDR-TB cases*

**30 high-burden countries**

Incidence rates, 2015

*Estimates, new cases per 100,000 population*

- 40 - 99
- 100 - 199
- 200 - 299
- 300 - 499
- 500+

Source: WHO global tuberculosis report 2016
MENA region: prevalence of multidrug-resistant TB

Source: http://www.emro.who.int/entity/statistics/country-health-profiles.html
The MENA region is among the countries with highest rates of ESBL-producing *Enterobacteriaceae*

ESBL spread in MENA region:
- ESBL producing *K. pneumoniae*: up to 80%
- ESBL producing *E. coli* up to 70%

Source: Arab Alliance for Prudent Use of Antimicrobial 2014
Antibiotic resistant *E. coli* in Qatar

Source: Dr. Emad Ibrahim, HMC Microbiology and Virology Division, 2017, unpublished data
The WHO has recently published the foremost list of antimicrobial resistant “priority pathogens” including: *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter*.

**ESBL-producing *Enterobacteriaceae*** is considered by WHO as among the six drug-resistant pathogens for which there are few potentially effective drugs, complicating the treatment of serious hospital-acquired infections.

November 2012-October 2013, we conducted a prospective study on routine specimens received at the Microbiology Lab (HMC), from patients admitted to intensive care units (ICUs) at HMC.

A total of 629 *Enterobacteriaceae* isolates (a single isolate per patient) were collected from various clinical specimens as part of routine clinical care.
ESBL-producing *Enterobacteriaceae* prevalence rate in tested isolates = 17.3%.

Amongst the isolates, *K. pneumoniae* (51.4%) was the most common, followed by *E. coli* (34.7%).
Antimicrobial susceptibility profile of the ESBL producing *Enterobacteriaceae* isolates

- Intermediate resistance:
  - 99.4% Ciprofloxacin (CI)
  - 33.0% Gentamicin (GM)
  - 35.8% Tigecycline (TGC)
  - 61.5% Trimethoprim/Sulfamethoxazole (TS)

- High resistance to β-lactam antibiotics:
  - 99.1% for Amoxicillin/clavulanic acid combination (AMC)
  - 99.1% for Ceftriaxone (CRO)
  - 93.6% for Cefepime (PM)
Molecular genotyping of ESBL-producing isolates

- Most ESBL enzymes belong to **TEM** (Temoneira), **SHV** (sulphydryl variable), or **CTX-M** (cefortaxime-hydrolyzing β-lactamase) family of enzymes.

- **CTX-M** was the most prevalent type (66.1%) in our tested isolates, followed by **SHV** (53.2%) & **TEM** (40.4%).

- 24.7% of the strains showed presence of all three *bla* genes (**TEM**/**SHV**/**CTX-M**).

- 46.4% of *Klebsiella pneumoniae* isolates were found to carry genes for all the three types of ESBL’s.
The emergence of Multidrug-Resistant *Pseudomonas aeruginosa* (MDR-PA) from 5 independent hospitals in Qatar

• Worldwide, *P. aeruginosa* is the second most common GNB isolated from healthcare-associated infections.

• Several studies described a significant and alarming increase in Multidrug-Resistant (MDR)* P. aeruginosa.*

• Although *P. aeruginosa* is the 2nd most encountered GNB at HMC, the epidemiology of MDR-PA has not been described clearly in Qatar.

• During the period between Nov. 2014 to Oct. 2015, a total of 2533 *P. aeruginosa* isolates were collected from patients attending ambulatory clinics/admitted to the acute care units of 5 different hospitals serviced by the HMC.

• The overall percentage of MDR-PA* was 8.1% (n=205/2533) in this study.

* MDR-PA is defined as resistance to at least one antibiotic from ≥3 antipseudomonal classes.
Susceptibility patterns of *P. aeruginosa* isolates from Qatar

- The isolates showed high resistance to all antibiotics tested (cephalosporin, aminoglycoside, fluoroquinolone, Penicillin+beta lactamase inhibitor, carbapenem) except colistin: = MDR-PA

- Five *Pseudomonas aeruginosa* isolates were resistant to all antibiotics tested, including colistin: = Pan Drug Resistant *Pseudomonas aeruginosa* (PDR-PA).

Legend:
- FEP: Cefepime
- GEN: Gentamicin
- CIP: Ciprofloxacin
- TZP: Piperacillin-tazobactam
- AMK: Amikacin
- MEM: Meropenem
- CST: Colistin
- TOB: Tobramycin
Susceptibility of *P. aeruginosa* isolates in Qatar to recently FDA-approved antibiotics

- 22.4% of the *P. aeruginosa* isolates in our study are resistant to Ceftazidime/Avibactam (CAZ-AVI), and Ceftolozane/Tazobactam (C/T).

**Legend:**
- **CAZ-AVI:** Ceftazidime/Avibactam
- **C/T:** Ceftolozane/Tazobactam
- **FEB:** Cefepime
- **GM:** Gentamicin
- **CIP:** Ciprofloxacin
- **PIP/TAZ:** Piperacillin/tazobactam
- **AK:** Amikacin
- **MER:** Meropenem
- **CS:** Colistin
- **TOB:** Tobramycin
Efforts to Combat Antibiotic Resistance

Superheroes vs. Superbugs

STOP THE SPREAD OF NEW ANTIBIOTIC RESISTANT BACTERIA.

LET THEIR FORCE BE WITH YOU... WHEN YOU REALLY NEED IT!

FOR MORE INFORMATION, VISIT WWW.ISGLOBAL.ORG
Impact of antibiotic resistance

- Higher patients mortality.

- Increased hospital stays and costs: e.g., a case-control study (Slama T, 2008)
  - ESBL-Enterobacteriaceae infection cases:
    - Mortality (35%);
    - Longer hospital stay (11 days).
    - Hospital costs of $46,970/patient.

  - Control cases (bacteremia due to non-ESBL strains)
    - Mortality 18%;
    - Shorter hospital stay (5 days).
    - Hospital costs of $16,877/patient.

- Significant cost impact in developing new antibiotics (currently estimated at $1 billion/drug).

- Increased implementation costs of surveillance and antimicrobial stewardship programs.
Fighting Back!

• In 2013, the CDC has published a report recommending 4 necessary actions to prevent antimicrobial resistance:

  1. Prevent infections, and prevent the spread of resistance (in hospitals, in the community, and in food).
  2. Tracking resistance patterns.
  3. Improving antibiotic prescribing and use via implementation of antimicrobial stewardship
  4. Developing new antibiotics and diagnostic tests.

Global initiatives to combat AMR

• **2014:** WHO Global Report on Antimicrobial Surveillance:
  - Very high rates of resistance observed in healthcare- and community-associated infections in all WHO regions.
  - Significant gaps in surveillance.
  - And the report concluded; with an urgent need to strengthen collaboration on global surveillance on AMR.

• **August 2014:** USA President Executive Order, followed by White’s House National Strategy to Combat Antibiotic-Resistant Bacteria (create programs & funds to deal with antibiotic-resistant bacterial infections).

• **May 2015:** World Health Assembly endorses "Global Action Plan* to tackle AMR.

• **EU Commission Action Plan (2011-2016)** against the rising threats from AMR.

• **May 2016:** UK Government calls for urgent action in response to Lord Jim O’Neill’s independent review of antimicrobial resistance in collaboration with the Wellcome Trust.

• **September 2016:** 193 leaders sign UN Declaration to take action on AMR, reaffirming their commitment to develop national action plans on AMR, based on the global action plan.
Global Action Plan on AMR

- Adopted in the 68th World Health Assembly in May 2015.

Global Action Plan: Priority areas
Members States to develop National Plans on Antimicrobial Resistance by May 2017

1. Improve awareness and understanding of AMR
   - Risk communication
   - Education

2. Strengthen knowledge through surveillance and research
   - National AMR surveillance
   - Laboratory capacities
   - Research and development

3. Reduce the incidence of infection
   - IPC in health care
   - Community level prevention
   - Animal health: prevention and control

4. Optimize the use of antimicrobial medicines
   - Access to qualified antimicrobial medicines, regulation, AMS
   - Use in veterinary and agriculture

5. Ensure sustainable investment in countering AMR
   - Measuring the burden of AMR
   - Assessing investment needs
   - Establishing procedures for participation

Antimicrobial Stewardship

https://www.google.com/search?q=Antimicrobial+stewardship+program&source=
Describe your role in the Antimicrobial Stewardship Program (ASP) at your institution

A. I’m formally involved at greater than 20% of my effort
B. I’m formally involved at less than 20% of my effort
C. I’m not formally involved in our ASP
D. What is an ASP?
Antimicrobial stewardship

- **Definition**: “coordinated interventions designed to improve and measure the appropriate use of antibiotic by promoting the selection of the optimal antibiotic regimen including dosing, duration of therapy, and route of administration”.

- **Objectives**:
  - Improve patient outcomes.
  - Avoid harm from adverse reactions, drug allergies, and adverse events such as *C. difficile* infection.
  - Improve rates of antibiotic susceptibilities to targeted antibiotics.
  - Decrease antimicrobial resistance.
  - Optimization of resources utilization.

* (IDSA, PIDS, SHEA)
Core elements of hospital antimicrobial stewardship programs

1. Leadership Commitment
2. Accountability
3. Drug Expertise
4. Action
5. Tracking
6. Reporting
7. Education

Stewardship mechanisms of action

• **Restrictive:**
  - ASP uses this strategy to either prevent or provide a barrier to over-prescribing or mis-administration of antibiotics. This includes; pre-authorization, and removal by restriction.

• **Persuasive:**
  - A persuasive strategy uses interventions that attempt to persuade health-care professionals to prescribe appropriately by: education, reminders, audit, and feedback.

• **Structural:**
  - This strategy includes introduction of rapid diagnostic technology or computerised clinical decision support, for enabling physicians to initiate early and ideal antimicrobial therapy.

• **Pharmacy interventions:**
  - Pharmacist-initiated interventions include recommendations such as; changing the treatment duration, switching patients from I.V. to oral therapy, and using a narrower-spectrum antibiotic.
HMC launched the Antimicrobial Stewardship as a pilot in March 2015, and structured across HMC by July 2017*.

The program aims to monitor antibiotic usage and to combat antimicrobial resistance at the hospital level.

Mechanism of action: restriction and pre-authorization as a front rule end.

The program involves many interventions including education of physicians on the proper use of antibiotics, infection control, and enforcement of the antibiotic restriction policy in Qatar.

*Source: Dr. Hisham Ziglam, ID Senior Consultant, and Director of ASP at HMC
Effect of implementation of antimicrobial stewardship program in HMC on MDR-PA prevalence

• MDR-\(P.\) aeruginosa has decline from 8.1% in 2015 to 4.9% in 2017.

Source: HMC Antimicrobial Stewardship Program
Do you have the next antibiotic?

Being antibiotic resistant is the best.

Yup.

They're not going to find better antibiotics, will they?

Nope.

I dunno... Sometimes I worry there's something that will kill us all just sitting on a shelf somewhere.

Hm.

Eh, they'd have to test so much stuff to find new antibiotics, though.
History of antibiotic discovery

1880- Erlich & Dyes (salvarsan)
1928- Fleming & Penicillin
1932- Domagk & Sulfonamides
1943- Waksman & Streptomycin

Number of new systemic antibacterial agents approved by the FDA per 5-year period (Choffnes, et al., 2010)
Antibiotic discovery methods

**Traditional Antibiotic Search**
- Soil is cultured directly onto culture medium
- Yields 1% bacterial recovery

**iChip-based Antibiotic Search**
- The iChip is seeded with soil dilutions such that an average of one bacterial cell is placed in each microchamber; the iChip is then placed back into soil
- Colonies are cultured and grown, with up to 40% bacterial recovery

**Next steps:**
- Optimize growth of organisms
- Recover cell extracts
- Test against bacteria
- Purify active compounds

Source: Cesar A. Arias & Barbara E. Murray, 2015
**Objective:** To discover novel antibiotics by using a microfluidics platform.

**Methodology:** An integrated ultra high throughput microfluidic platform "PolyChip" will be used to support the identification and analysis of antimicrobial products generated by both culturable and unculturable microbes in direct functional bioassays with pathogens of high interest.
Functional components of the PolyChip

Droplet Generation

Droplet Merging

Droplet Synchronization

Droplet Mixing

Droplet Culture

Droplet Sorting

Electrode

Droplet Generation

Droplet Merging

Droplet Mixing

Co-Cultivation

Oil Inlet

Media Inlet-1

Media Inlet-2

Electrode

Pneumatic Valves

Outlet 1

Outlet 2

Waste

PMT

Optical Fiber

LED/Laser

Cell Inlet

Oil Inlets

Cell Inlet

400 µm

400 µm

400 µm

400 µm
Benefits and significance of the PolyChip approach

• Allow high throughput screening of environmental microbes for production of antimicrobials with at least four orders of magnitudes improvement, compared to conventional co-cultivation methods.

• Allow for a much larger screening body than just culturable microbes due to direct on-chip short co-culture conditions, and incorporation of soil extract media.

• It will also provide single-cell resolution, thus establishing a new paradigm in antimicrobial drug discovery.
Take Home Message

• Antibiotic resistance is here, is spreading, and is serious!

• Partnerships and collaborations between the stakeholders are urgently needed and should be encouraged.

• Antimicrobial stewardship programs when correctly implemented, are very effective in reducing spread of drug resistance.

• Research and development for new antibiotics is critical in future fights against drug-resistant microbial infections.
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Questions?
Polychip current status

• **Device**
  – Device fabrication is in process.

• **Optical detection is the final hurdle**
  – Challenge 1: Various dyes were tested and these did not work due to lack of specificity or high background noise
  – Challenge 2: GFP-labeled cells show weak fluorescence under LED excitation
  – Solution: Moving to laser-based excitation (confirmed using conventional laser fluorescent microscope that high laser light intensity results in very strong emission) => currently in the process of purchasing a laser and relevant filter sets
Common associated underlying conditions of MDR-PA infections in Qatar
The chaos of antibiotics prescribing

• People take antibiotics for knee pain, for runny noses,”. "Doctors are under a lot of pressure from the patients to prescribe antibiotics, because if the patient doesn't receive antibiotics, the patient will not go back to the doctor.”

• "Even doctors write prescriptions for antibiotics without knowing if [an infection] is viral or bacterial," and patients often don't complete prescribed courses of antibiotics, stopping as soon as they feel better.

• Even without a prescription, a person can walk into a pharmacy, present symptoms or a self-diagnosis—"Good afternoon, I believe I have a urinary-tract infection"—and the pharmacist will most likely hand over some affordable packs of antibiotics.

• In this perfect storm of relaxed policy, lack of awareness, and doctors and pharmacists worried about making money, the lax dispensation of antibiotics and their consequent abuse is a recipe for disaster.

Multi-Drug Resistant (MDR)/Extensively drug-resistant (XDR)/Pan-drug-resistant (PDR)

- **MDR**: Bacteria with resistance to antibiotics in three or more classes of antibiotics will be classified as multi-drug resistant.

- **XDR**: Bacteria with non-susceptibility to at least one agent in all, but two or few classes will be defined as extensively-drug resistant.

- **PDR**: Bacteria with non-susceptibility to all agents in all classes will be classified as pan-drug resistant.