Global Leaders Group on Antimicrobial Resistance
Forging partnerships between science and policy
A view from India
Lessons from COVID-19 in India

Fear drives over-treatment, particularly when drugs are accessible and there are no negative consequences for irrational therapy

- May 2021 Prescription for SPO2 of 96
  - Home care, rest and fluids
  - Tab Ivermectin 12 mg after dinner for 5 days
  - Tab HCQS 400 BD for one week than once daily
  - Tab Fabiflu 1800 mg twice at 12 hr interval followed by 800 mg twice daily after meals for 7 days
  - Tab Doxy 100 mg twice daily after meals for 7 days
  - Tab Placef 200 mg twice daily for 10 days
  - Tab Famotidine 150 mg twice daily before food for 2 weeks
  - Tab Allegra once daily 3 weeks
  - Tab Nucoxia P three times after food ten days
  - Tab Ecosprin 75 once daily after food 6 weeks
  - Cap Zincovit twice daily 2 weeks after breakfast and dinner
  - Cap Limcee twice daily 2 weeks after breakfast and dinner
  - Tab Calpol 650 sos for fever

Source: BBC
Overuse of drugs can have unintended consequences

‘Black fungus’ during Covid-19

- Not seen elsewhere in the world
- Different rates in northern/southern India
- In northern India, >30,000 reported cases
- In our hospital
  - 4 cases in hospitalized COVID-19
  - All treated with steroids outside hospital

What does irrational antibiotic use mean for AMR?
The access and excess story

- Infant mortality rate in India has declined from 125 per 1000 live births to <20 per 1000 live births in the state of Tamil Nadu, similar but not as sharp a decline in the rest of India.
- Perinatal and neonatal deaths contribute to 40-60% of infant mortality.
- Neonatal sepsis is high, driven mostly by Gram negative organisms, with high rates of resistance particularly *Klebsiella pneumoniae*, *Escherichia coli* and increasingly *Acinetobacter*.

- Community based antibiotic use in under 5 children in India:
  - 64% of respiratory infections by Day 3
  - 67% fever by Day 3
  - 35% diarrhea by Day 2
Antibiotics are used everywhere
One Health and AMR
Antibiotic resistance in the food chain

- Animal-human mixing patterns are different between industrialised and low- and middle-income countries
  - Household animals, small-scale backyard poultry and dairy farms and herds, as well as larger scale commercial poultry
- Colistin resistant bacteria reported in India in meat, mutton, fish, fruits and vegetables in 2018
- China exported approximately 100 metric tonnes of colistin-premixed animal feed, supplements and additives per year (2016-2018) to India
  - China reported mcr-1 in 2016 in food samples and banned the use of colistin in food animals
- Prompted a deeper dive into sources
  - Colistin-containing feeds (older brand names Coligro-100, Progrovet, newer unbranded feeds) marketed for treatment and prevention of bacterial infections and as antibiotic growth promoter for better feed conversion and increased weight gain in broilers
  - Colistin banned in 2019
- Complicated picture
  - New genomic studies indicate separation between resistance patterns and mechanisms between animals and humans in India at least in cross-sectional data (V. Balaji, CMC Vellore)
  - But data from other enteric pathogens indicate frequent transmission of bacterial, viral and parasitic species between animal and humans living in close proximity
In this situation, what tools do we have?

- Restriction of antibiotics
- Rational use, including cycling
- Infection prevention and control
- Vaccines
Typhoid remains familiar in public perception
But the medical profession and policy makers think typhoid does not need interventions beyond antibiotics

- Older cohort studies show high incidence of typhoid esp. in young children, no recent studies until 2016
- Decline in typhoid isolation at tertiary care facilities

Typhoid genomics

S. Typhi - A single dominant MDR lineage “H58” that has emerged and spread throughout Asia and Africa over the last 30 years

Temporal distribution of S.Typhi Genotypes

Major geographical transfers within the H58 lineage – South Asia (Hub of H58)

Unique lineage of H58 S. Typhi

Emergence of an Extensively Drug-Resistant *Salmonella enterica* Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins

Elizabeth J. Klemm,a Sadia Shakoor,b Andrew J. Page,a Farah Naz Qamar,b Kim Judge,a Dania K. Saeed,a Vanessa K. Wong,c Timothy J. Dallman, a Satheesh Nair, b Stephen Baker,c,d Ghazala Shaheen,b Shahida Qureshi,b Mohammad Tahir Yousafzai,b Muhammad Khalid Saleem,b Zahra Hasan,b Gordon Dougan,a,e Rumiha Hasanb

a. b.

The H58 clade spread from India in the late 1980s

The Pakistan H58 has both plasmid- and chromosomally mediated resistance genes
Incidence in children
1170/100,000 child years of observation
In some locations 80% of children were on antibiotics by Day 3 of fever, whether or not typhoid was proven.
The international and intercontinental spread and expansion of antimicrobial-resistant *Salmonella Typhi*: a genomic epidemiology study. Da Silva et al, Lancet Microbe 2022
Different vaccination strategies: 10-year incidence projections

- Routine urban + campaign
- Routine all + campaign
- Status quo
National Rotavirus Surveillance

37% of all children hospitalized with diarrhoea have rotavirus
Impact of rotavirus vaccine after introduction into the universal immunization programme in India, pre-vaccine and post-vaccine introduction surveillance comparison

Overall reduction of diarrhoea by 20-30%. Two fewer courses of antibiotics in infancy
Science and policy summary

- Irrational antibiotic use was highlighted during COVID and continues to be a problem in LMICs
- Solving for both access and excess is necessary (neonatal infections)
- Some interventions have had effects (ban colistin in food animals, IPC where implemented consistently), not others (other antibiotics in animal feeds, red line)
- Vaccines hold potential for lowering antibiotic use and hence decreasing AMR