Are we facing a superbug apocalypse?  
- the Antibiotic Paradox

"Don’t it always seem to go  
That you don’t know what you’ve got till it’s gone”
Joni Mitchell (1970), Big Yellow Taxi

fast forward to 2013

Antibiotic resistance: a final warning
The Lancet  | Sep 28, 2013
We are rapidly approaching the point when antimicrobial resistance will be nothing short of a catastrophe. And for the many thousands in the USA and elsewhere, the world’s response is already too late.

US: 4.6% of global population, 46% of global ab market  
CDC: resistant organisms → infections in >2 million, 23,000 deaths in US each year

“A post-antibiotic era means, in effect, an end to modern medicine as we know it.....

..... Some interventions, like hip replacements, organ transplants, cancer chemotherapy and care of preterm infants, would become far more difficult or even too dangerous to undertake”

Dr. Margaret Chan, director general WHO. March 16, 2012
Blood stream infections:
- Enterobacter cloacae x 1
- Enterobacter cloacae (ESBL) x 1
- MRSA x 2
- Pseudomonas aeruginosa x 2
- A baumannii (MRAB) x 2
- Klebsiella pneumoniae (ESBL) x 1
- Enterococcus faecalis x 1
- Providencia sp x 1
- Candida parapsilosis (yeast) x 1

Outcome measure 1:
- ICU: Patient survival = success ++

Outcome measure 2:
- ID/Micro: 130d: ICU, Burns, MRO exposure ++, Antibiotic use ++ = infection control disaster

>50% antibiotic use in hospitals repeatedly shown to be inappropriate

antibiotic resistance is Darwinian, BUT
- few new drugs in the development pipeline
eg. 15/18 major pharma suppliers have left antibiotic field*

Bartlett JG, Clin Infect Dis, 2013


“the etiquette of antibiotic prescribing”

individual patient care approach
- 'just in case' it is infection (defensive prescribing)
- risk of individual failure >> long-term loss of efficacy
- more antibiotics, longer duration, broader is safer vs.
societal approach
- attempts to conserve antibiotics, 'stewardship'
- avoid collateral selection (resistant organisms, C.difficile, )
- against law of entropy?

The discovery dates of distinct classes of antibiotics. No new classes have been discovered since 1987.

one slide crash course about “Superbugs”??!!

- some bacteria are antibiotic susceptible but ‘virulent’.
- some are resistant but cause infection only in a small minority
- bacteria are part of our ‘commensal’ flora.
  - Staph on skin, E.coli as part of gut flora
  - Gram- (E.coli) also in other niches: animals, food, environment
- bacteria transfer genetic material very efficiently
- codes for resistant enzymes → protect bacteria from antibiotics
- the more antibiotics inhibited, the more ‘multiresistant’
- some confer extreme resistance & risk of untreatable infection:
  - ESBLs:
  - CREs (NDM, KPC)

eg. Staph
eg. E.coli, Klebsiella

THE BLACK PLAGUE

Spread by merchants and travelers, the plague killed > 1/3 of Europe’s population within 5 years

**Klebsiella pneumoniae** in blood cultures resistant to 3rd Gen Cephalosporins (cefotaxime/ceftriaxone)


**Trends in MRSA and ESBL E.Coli bacteremia in Europe.**

- 2.5 x 30 day & 2.9 x hospital mortality

resistant infections associated with higher rates of death, illness and prolonged hospital stay

- India makes ~ 1/3 world’s antibiotics ($12.4 billion)
- 5,000+ manufacturers of generic antibiotics
- 23% of city dwellers have no toilets 2012 WHO report
- In 2007 ~45,000 cipro doses released daily downstream of Hyderabad sewage plant
  "India has lost the war against the toughest forms of antibiotic resistance, largely because of poor sanitation, unregulated use of antibiotics and an absence of drug resistance monitoring."
- >100 million NDM-1 +ve in India
- Pakistan hospitals: 37% CRE+

**Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study**

171 environment swabs - 51/171 (29.8%) NDM-1+
50 water samples - 2/50 (4%) NDM-1+

**THE WALL STREET JOURNAL. INDIA**
As we start to understand the gut microbiome, are we creating genetically modified animals?

**Solutions**

- Smart companies and smart governments:
  - leadership / governance / political will
  - incentives to pharma
  - diagnostics, rewarding innovation

- Behavioural:
  - promote the special / fragile nature of antibiotics
  - identify personal and societal triggers to behaviour change

- Structural: hospitals (e.g., infection control), sanitation

- Organisational: engagement with all identified specialities, interest groups

- International: resistance does not respect borders

- Legislative: worldwide ban on non-therapeutic use in animals

- Sustained: the world has a short attention span
Competition for government commitment

Antibiotic resistance
• an intangible problem
c/w obesity, cardiac disease, mental illness ...
• like climate change ? seen as someone else’s problem to tackle, even within medical specialities
• role of outside factors - can local investment turn things around without international commitment
• AMRSC, MBI

“... as in state affairs, by foreseeing them at a great distance, the evils which might arise from them are soon cured;
- but when from want of foresight, they are suffered to increase to such a height that they are perceptible to everyone, there is no longer any remedy”

Niccolo Machiavelli in “The Prince” (1513)