



## Competing priorities

Antibiotic use in a time of increasing antibiotic resistance

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February 14, 2018



## Today

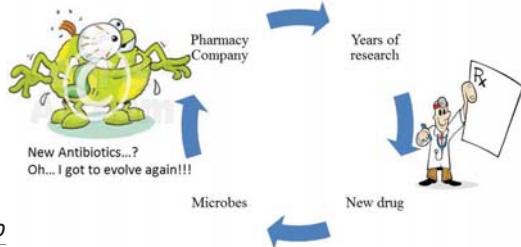


Funding for this project has been provided by Virginia Ag Council & USDA NIFA award 2014-05280.



**Antibiotic resistance** a critical human health challenge, need “global strategy to contain resistance”

- 2 million Americans infected, 23,000 die/year

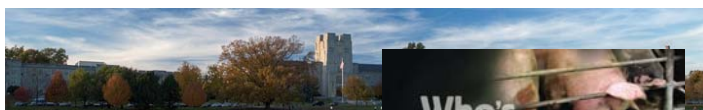


WHO, 2000



## Development of Antibiotic Resistance

Antibiotic	Discovery / 1 <sup>st</sup> clinical use	Resistance first observed
Penicillin	1940 / 1943	1940
Streptomycin	1944 / 1947	1947
Tetracycline	1948 / 1952	1956
Erythromycin	1952 / 1955	1956
Vancomycin	1956 / 1972	1987
Gentamicin	1963 / 1967	1970



“Sen. Floats Bill to Combat Antibiotic-Resistant Bacteria”

Antibiotics Have Gone From Wonder Drugs to Wonder-If-They'll-Work Drugs

**Antibiotic resistance 'crisis looms'**  
Superbug infections threaten 20th century's wonder drugs



Antibiotic resistance: The last resort

Health officials are watching in horror as bacteria become resistant to powerful carbapenem antibiotics — one of the last drugs on the shelf.

CDC Sounds Alarm on Antibiotic-Resistant Bacteria

Report cites overuse of antibiotics as key to the life-threatening problem

CDC Acknowledges Role of Farms in Antibiotic Resistance

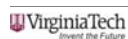
Disease resistance to antibiotics at tipping point, expert warns

Prof Jeremy Farrar says evolution of diseases will 'creep up on us' and affect patients in UK

FDA Underwhelms With Response to Super-Resistant Infections Rise

Antibiotics Warning: Resistance 'Growing'

**Is this criticism legit?**



## It's the manure.

- Key questions:
  - Dose vs. excretion?
  - Degradation during storage, treatment?
  - Persistence in soil
  - Runoff
- Actual risk to humans?





## Coming right out the other end...

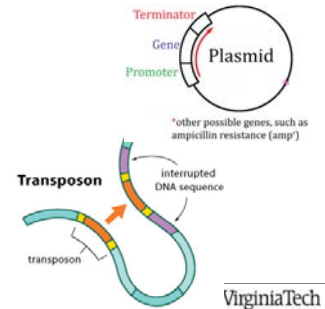


Antibiotic/class	% excreted
Beta lactams	Humans: 78-84%, urine ( <i>Weidekamm, 1984</i> )
ceftiofur HCl	Beef cattle: 31% in feces, 55% in urine ( <i>Beconi-Barker 1996</i> )
ceftiofur	Swine: 62% in urine, 11% in the feces ( <i>Hornish 2002</i> )
Avilamycin (glycopeptide)	Swine: 95% in feces ( <i>European Medicines Agency 2007</i> )



## Antibiotic resistance genes (ARG)

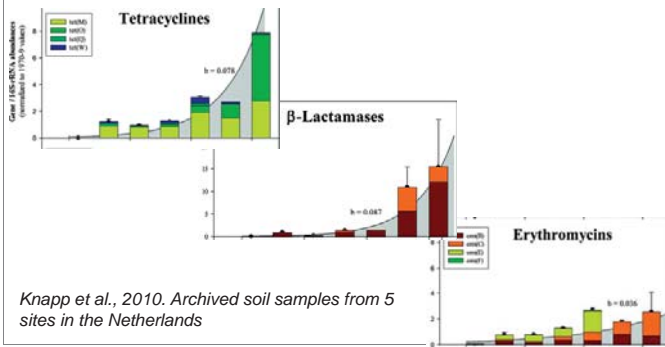
- Spontaneous or induced
- Bacteria carrying ARG can survive exposure to that antibiotic.
- Genes can be **swapped**, can travel **together**, and **outlive** bacteria.



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Invent the Future



## In soil? The 70's vs. 2008



## What about dairy?

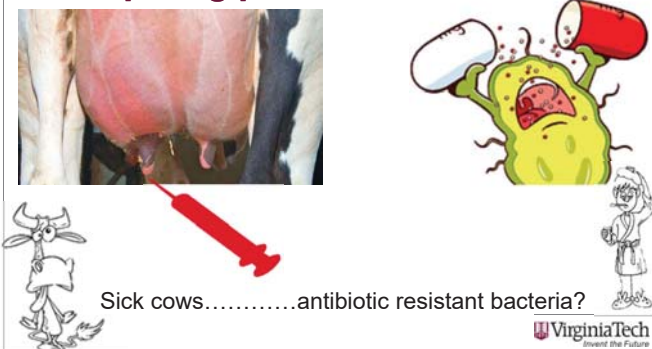
- Growth promotion
  - ionophores
- Prophylactic
  - Milk replacers
  - Dry cow therapy
- Therapeutic use



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## Competing priorities



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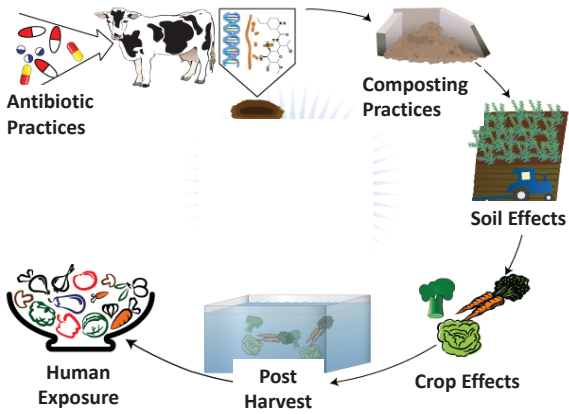
## Where we're going with this

- What cows?
- What manure?
- What days?
- Treated in what way?



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## USDA "Farm to Fork" AR Mitigation

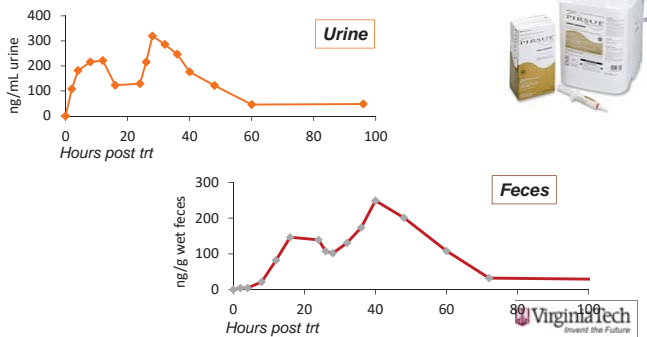


### It's the manure.

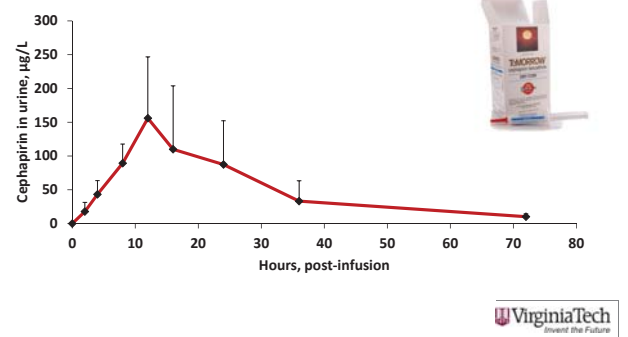
- Today:
  - Dose vs. excretion?
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### Excretion following trt?



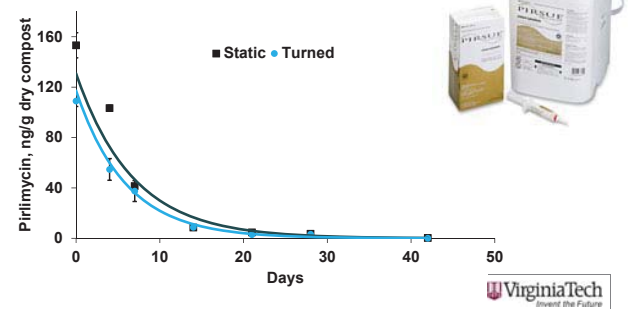
### Excretion following trt?



### Does excreted = environmental load?



### Fate of pirlimycin w/composting





### Fate of cephapirin w/composting



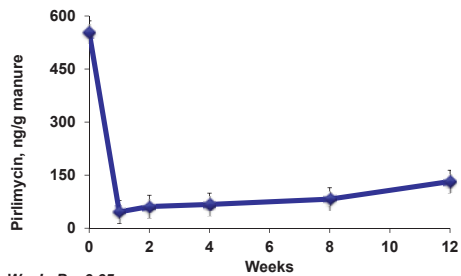
### ABX removal with composting

Manure	Drug	Removal	ref
Swine	CTC	100% by 21d	1
Swine	sulfadiazine	100% by 3d	1
Swine	ciprofloxacin	70-80% at 56d	1
Broiler	CTC	90% by 42 d	2
Layer	CTC	90% by 42d	2
Beef	CTC, OTC	99% by 30d	3
Broiler	OTC	84% at 20d	4
Dairy	Sulfamethazine	>95% at 28d	5

<sup>1</sup>Selvem et al, BRT 2012; <sup>2</sup>Bao et al, WM 2009; <sup>3</sup>Arakin et al., JHM 2009; <sup>4</sup>Ravindran et al., IJEST, 2017; <sup>5</sup>Mitchell et al., WASP, 2015



### Fate of pirlimycin during liquid storage



Week: P < 0.05

